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THE POTASSIUM SALTS OF FUMARIC ACID: PREPARATION, UNIT CELL CONSTANTS, SPACE GROUPS, AND X-RAY DIFFRACTION POWDER IDENTIFICATION DATA¹

M. P. GUPTA² AND W. H. BARNES

ABSTRACT

The preparation of the three crystalline potassium salts of fumaric acid, "acid" potassium hydrogen fumarate ($2\text{KHC}_4\text{H}_2\text{O}_4 \cdot \text{H}_2\text{C}_4\text{H}_2\text{O}_4$), potassium hydrogen fumarate ($\text{KHC}_4\text{H}_2\text{O}_4$), and dipotassium fumarate dihydrate ($\text{K}_2\text{C}_4\text{H}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$), is discussed, and suitable pH values for the growth of single crystals of each are given. Unit cell, space group, and X-ray diffraction powder identification data for the three salts are presented.

INTRODUCTION

There are three crystalline potassium salts of fumaric acid, $\text{K}_2\text{C}_4\text{H}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$, $\text{KHC}_4\text{H}_2\text{O}_4$, and $2\text{KHC}_4\text{H}_2\text{O}_4 \cdot \text{H}_2\text{C}_4\text{H}_2\text{O}_4$. The first two were prepared by Rieckher in 1844 (1), and all three were obtained by Carius in 1867 (2). Rieckher (1) saturated fumaric acid in water with potassium carbonate and allowed the aqueous solution to evaporate, thus obtaining the normal salt which he found to be a dihydrate from the loss in weight at 100°C ; by incineration to potassium carbonate he determined the formula as " $\text{KO}, \text{C}_4\text{HO}_3 + 2\text{Aq}$ " (i.e., $\text{K}_2\text{C}_4\text{H}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$). Potassium hydrogen fumarate was prepared from the neutral salt and acetic acid, from fumaric acid and potassium carbonate followed by the addition of more fumaric acid, and from the neutral salt and fumaric acid. Rieckher showed that crystals of potassium hydrogen fumarate are anhydrous, and, by conversion to potassium sulphate, he established the formula as " $\text{KO}, \text{C}_4\text{HO}_3 + \text{C}_4\text{HO}_3, \text{HO}$ " (i.e., $\text{KHC}_4\text{H}_2\text{O}_4$). Carius (2), apparently unaware of Rieckher's work, treated solutions of barium fumarate with potassium sulphate and various concentrations of sulphuric acid, and thus obtained not only the two salts to be expected of a dibasic acid but, in addition, an "acid" potassium hydrogen fumarate, $2\text{KHC}_4\text{H}_2\text{O}_4 \cdot \text{H}_2\text{C}_4\text{H}_2\text{O}_4$, which he first considered to be a monohydrate (2) but later (3) decided was anhydrous. His analysis of dipotassium fumarate was carried out after the compound was dried at 100°C so that his formula corresponds to that of the anhydrous salt and not to that of the dihydrate. Carius also observed, like Rieckher, that $\text{KHC}_4\text{H}_2\text{O}_4$ could be crystallized from a solution of $\text{K}_2\text{C}_4\text{H}_2\text{O}_4$ and fumaric acid, but he also reports (3) that it is not obtained from a solution of the former and "acid" potassium hydrogen fumarate, which recrystallize separately.

Dehn and Merling (4) prepared $\text{K}_2\text{C}_4\text{H}_2\text{O}_4$ (presumably anhydrous) from fumaric acid and potassium hydroxide in anhydrous ether. Zechmeister and Szécsi (5) obtained "acid" potassium hydrogen fumarate from an alcohol extract of *Capsella bursa-pastoris*, and also from the appropriate molar proportions of fumaric acid and potassium hydroxide.

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Finally, Sabalitschka and Kubisch (6) prepared potassium hydrogen fumarate from fumaric acid and *N*/2 KOH solution. All three salts are included in the 1893 and 1942 editions of Beilstein's *Handbuch* (although the latter gives the normal salt in its anhydrous form) but $2\text{KHC}_4\text{H}_2\text{O}_4 \cdot \text{H}_2\text{C}_4\text{H}_2\text{O}_4$ does not appear in the edition of 1920 (7).

Crystals of $\text{K}_2\text{C}_4\text{H}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$ are described by Rieckher (1) as "brilliant, short, striated prisms" and by Carius (3) as "bright, monoclinic prisms and plates". Rieckher (1) refers to crystals of $\text{KHC}_4\text{H}_2\text{O}_4$ variously as "clear and regular", and as "irregular needles", while Carius (3) describes them as "thick, monoclinic (?) plates". Crystals of $2\text{KHC}_4\text{H}_2\text{O}_4 \cdot \text{H}_2\text{C}_4\text{H}_2\text{O}_4$ are said by Carius (3) to be "needle-like prisms" and are referred to as "elongated and tapering" by Zechmeister and Szécsi (5). Optical crystallographic data are given by Repossi (8) (see also Groth (9)) for crystals of $\text{KHC}_4\text{H}_2\text{O}_4$ said to have been obtained from aqueous solution. Stafford (10) reports refractive indices for dipotassium fumarate but fails to indicate whether they are for the anhydrous salt or the dihydrate. Gupta (11) describes a preliminary investigation of the crystal structures of "acid" potassium hydrogen fumarate and of "acid" rubidium hydrogen fumarate which were prepared by the addition of fumaric acid to aqueous solutions of the appropriate hydroxides; the composition of the potassium salt was verified by an analysis for carbon and hydrogen. As Gupta points out, the composition of the potassium salt may be expressed as $2\text{KC}_4\text{H}_3\text{O}_4 + \text{C}_4\text{H}_4\text{O}_4$ or as $\text{K}_2\text{C}_4\text{H}_2\text{O}_4 + 2\text{C}_4\text{H}_4\text{O}_4$ but the two-dimensional structure analysis did not enable a choice to be made between the two formulations, if indeed there is any real difference between them. In the present paper the "acid" potassium hydrogen fumarate is designated by the first formula, namely $2\text{KHC}_4\text{H}_2\text{O}_4 \cdot \text{H}_2\text{C}_4\text{H}_2\text{O}_4$.

In anticipation of crystal structure investigations of $\text{KHC}_4\text{H}_2\text{O}_4$ and $\text{K}_2\text{C}_4\text{H}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$, crystals of all three salts have been grown from aqueous solutions of KOH or K_2CO_3 and fumaric acid, but it immediately became apparent that the particular salt obtained was dependent on the pH of the solution. An extensive series of crystallization experiments, therefore, have been carried out to establish suitable pH ranges within which satisfactory crystals of the various salts may be grown. Unit cell and space group data for $\text{KHC}_4\text{H}_2\text{O}_4$ and $\text{K}_2\text{C}_4\text{H}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$ have been collected, and indexed X-ray diffraction powder data for all three salts have been obtained.

PREPARATION

The potassium salts first were prepared by the addition of weighed amounts of pure fumaric acid to solutions containing previously weighed amounts of KOH or K_2CO_3 . The potassium fumarate solutions were boiled, filtered, and set aside to crystallize spontaneously and slowly in an air-conditioned room at 19 to 21° C and <50% relative humidity. The uncertain proportion of carbonate in solid KOH, and a significant proportion of hydrate (shown by X-ray powder photographs) even in fresh, unopened bottles of the highest grade of "anhydrous" K_2CO_3 , made it preferable to add measured volumes of a standardized solution of KOH (free from carbonate) to weighed samples of the fumaric acid; KOH is more satisfactory than K_2CO_3 because there is a tendency for KHCO_3 to crystallize first from the more strongly acid solutions. As soon as the approximate range of pH appropriate for the appearance of each fumarate had been determined, solutions were prepared by dissolving fumaric acid in *N*/10 KOH solution (carbonate free) and adjusting the pH to within the range desired. Universal indicator papers (such as Cenco pHDrion) are adequate for following the changes in pH although a Beckman pH meter with external electrodes is more satisfactory.

When crystals appeared, the solutions were tested for pH and the crystals were removed with tweezers, rolled gently on absorbent (bibulous) paper, and allowed to air-dry.

Distilled water was added to the solution, which was warmed to accelerate solution of unremoved crystals, and the beaker was set aside until the next small crop of crystals was obtained. This procedure was repeated until the volume had been reduced usually to a few drops. The solution was then allowed to evaporate to dryness and the solid residue was ground and mixed thoroughly. Representative crystals from each crop, and samples of the final residues, were identified by X-ray powder photographs.

The standard powder patterns employed for identification purposes were authenticated as follows: $2\text{KHC}_4\text{H}_2\text{O}_4 \cdot \text{H}_2\text{C}_4\text{H}_2\text{O}_4$, from data given by Gupta (11) for material analyzed for carbon and hydrogen; $\text{KHC}_4\text{H}_2\text{O}_4$, material analyzed for carbon and hydrogen; $\text{K}_2\text{C}_4\text{H}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$, crystallized from solution containing excess KOH, 4 g (air-dried at 19°C and 60% relative humidity) showed a loss in weight of 15.80% after heating to constant weight at 150°C (calculated for conversion of dihydrate to anhydrous salt, 15.78%). The authenticity of the standard patterns for $\text{KHC}_4\text{H}_2\text{O}_4$ and $\text{K}_2\text{C}_4\text{H}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$ later was confirmed by successful indexing on the basis of the unit cell and space group data.

No difficulty was experienced in the preparation of $\text{K}_2\text{C}_4\text{H}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$. The solubility was determined gravimetrically as approximately 62.4 g *anhydrous* $\text{K}_2\text{C}_4\text{H}_2\text{O}_4$ per 100 ml H_2O at 21°C ; the pH of a saturated solution at this temperature is about 10. Because of the high solubility, several recrystallizations under conditions of greatly reduced evaporation at room temperature were frequently necessary to obtain well-formed single crystals of reasonably small dimensions.

"Acid" potassium hydrogen fumarate is much less soluble in water (approximately 2.01 g $2\text{KHC}_4\text{H}_2\text{O}_4 \cdot \text{H}_2\text{C}_4\text{H}_2\text{O}_4$ per 100 ml H_2O at 21°C), and the pH of a saturated solution at 21°C is about 3.2. If the appropriate volume of standard KOH added to a weighed amount of fumaric acid is not sufficient for complete solution of the fumarate, water may be introduced until all solid has dissolved. Spontaneous crystallization by slow evaporation at room temperature usually gave good acicular single crystals. An annoying feature of solutions of this salt, however, was a propensity for nurturing the growth of mold over the sometimes long periods of evaporation necessary for the growth of the best crystals; this can be prevented by the addition of one or two drops of dilute formaldehyde solution. On a few occasions, crystals of fumaric acid (easily recognizable as opaque, feathery clusters) preceded the appearance of the first crystals of "acid" potassium hydrogen fumarate, particularly when the initial pH of the solutions was less than 3.0. The solubility of fumaric acid was determined gravimetrically as approximately 0.51 g $\text{H}_2\text{C}_4\text{H}_2\text{O}_4$ per 100 ml H_2O at 21°C ; the pH of a saturated solution at this temperature is about 2.2.

On the evaporation of a solution containing the proper proportions of fumaric acid and KOH (or K_2CO_3) to give $\text{KHC}_4\text{H}_2\text{O}_4$, the first crystals to appear are those of $2\text{KHC}_4\text{H}_2\text{O}_4 \cdot \text{H}_2\text{C}_4\text{H}_2\text{O}_4$. As crystallization of this salt proceeds, the pH of the solution rises until it approaches about 3.7, when crystallization of "acid" potassium hydrogen fumarate is replaced by that of $\text{KHC}_4\text{H}_2\text{O}_4$, which continues until the pH has risen to about 5. As evaporation proceeds to dryness, and the pH continues to rise, crystals of $\text{K}_2\text{C}_4\text{H}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$ appear. Similarly, when crystals of $\text{KHC}_4\text{H}_2\text{O}_4$ are dissolved in water, and the solution is allowed to evaporate, the same sequence of crystal identities and increasing pH is observed. Mold growth was troublesome in the acidic stages of these tests also until a drop or two of dilute formaldehyde was added to the initial solutions.

For the preparation of the potassium salts of fumaric acid, therefore, it is recommended that pure fumaric acid be dissolved in measured volumes of a standard KOH solution (free from carbonate) and that the pH of the solutions be adjusted to, and maintained at,

about 3.3 for $2\text{KHC}_4\text{H}_2\text{O}_4 \cdot \text{H}_2\text{C}_4\text{H}_2\text{O}_4$, about 4 for $\text{KHC}_4\text{H}_2\text{O}_4$, and about 8 for $\text{K}_2\text{C}_4\text{H}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$. The first and last may be recrystallized directly from water, but, after dissolving $\text{KHC}_4\text{H}_2\text{O}_4$ in water, the pH must be increased to about 4 in order to suppress crystallization of "acid" potassium hydrogen fumarate. The great difference in the solubilities of "acid" potassium hydrogen fumarate and dipotassium fumarate dihydrate should be kept in mind when one is selecting the initial volume of KOH solution for a

TABLE I
Single-crystal data for (A) $2\text{KHC}_4\text{H}_2\text{O}_4 \cdot \text{H}_2\text{C}_4\text{H}_2\text{O}_4$,
(B) $\text{KHC}_4\text{H}_2\text{O}_4$, (C) $\text{K}_2\text{C}_4\text{H}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$

	A	B	C
a (Å)	7.48	6.95 ₂	6.35 ₄
b (Å)	8.73	7.48 ₃	18.22 ₂
c (Å)	6.96	6.24 ₆	7.27 ₂
α	114° 18'	107° 05'	90° 00'
β	101° 54'	117° 00'	98° 20'
γ	98° 00'	96° 04'	90° 00'
Space group	$P\bar{1}$	$P\bar{1}$ (probable)	$P2_1/c$
Z (molecules per cell)	1	2	4
ρ_{calc} (g/ml)	1.796	1.927	1.819
ρ_{obs} (g/ml)	1.785	1.936	1.817

TABLE II
X-Ray diffraction powder data for $2\text{KHC}_4\text{H}_2\text{O}_4 \cdot \text{H}_2\text{C}_4\text{H}_2\text{O}_4$ (indexed for $d > 2.30$ Å)

d (Å)				d (Å)				d (Å)	
I/I_1	Obs.	Calc.	hkl	I/I_1	Obs.	Calc.	hkl	I/I_1	Obs.
20	7.76	7.70	100	20	2.82	2.83	11 $\bar{2}$	10	1.90
20	7.14	7.08	010			2.82	121	5	1.88
18	6.40	6.38	001			2.81	2 $\bar{1}$ 1, 01 $\bar{2}$	8B	1.84
	*	6.06	10 $\bar{1}$			2.77	12 $\bar{2}$	10B	1.81
		6.02	110	1B	2.76	2.74	301	10	1.78
30	5.46	5.46	111			2.73	22 $\bar{2}$, 12 $\bar{1}$	10	1.74
1	5.02	4.99	011			2.64	102, 310	8	1.70 [†]
		4.66	110	15	2.65	2.62	121	10	1.68 [†]
		4.52	01 $\bar{1}$			2.60	312	1	1.64
		4.24	101			2.59	321	1	1.62
	*	4.06	211, 11 $\bar{1}$	45	2.56	2.57	300	1	1.60
20	3.98	3.97	201			2.54	211	1	1.58
55	3.87	3.85	200			2.53	212	10	1.46
		3.81	210	10B	2.48	2.50	022	1	1.43
	*	3.76	111			2.48	112	1	1.41
		3.58	120			2.47	112	1	1.38
100B	3.56	3.54	121, 020			2.46	302, 131	2	1.36
		3.53	111	10	2.44	2.44	130	1	1.34
75	3.41	3.40	102			2.42	322	2	1.32
5	3.35	3.36	112			2.41	221	1	1.27
	*	3.24	021	60	2.39	2.40	231	2B	1.25
		3.20	221			2.38	320	5	1.22
15	3.20	3.19	002			2.36	030	8	1.20
15	3.14	3.14	212	1	2.34	2.33	220	2	1.14
20	3.09	3.07	210, 21 $\bar{1}$			2.32	311	2	1.12
		3.03	202			2.28		1	1.08
45	3.04	3.02	012	20B	2.16	20		2	1.06
		3.01	220	15	2.13	15		2	1.05
	*	2.97	02 $\bar{1}$	15	2.06	15		1	1.03
		2.95	120	10	2.02	10			
		2.88	201	25	1.99	25			
2	2.89	2.87	311	2	1.97	2			

*Reflection probably present but with $I/I_1 < 1$.

[†]Broad band; I/I_1 varies from 8 at edge corresponding to $d = 1.70$ Å to 10 at edge corresponding to $d = 1.68$ Å.

given preparation. Adjustment of pH upwards may be effected by the addition of KOH solution; if the solutions are not to be evaporated to dryness, dilute acetic acid may be employed for lowering the pH. In all cases, a few representative crystals from each crop should be ground and an X-ray powder photograph taken, for identification purposes, and to confirm that crystals of one salt only are present.

The foregoing notes throw light on some of the statements appearing in the early literature. Thus when Carius (3) recrystallized mixed solutions of $K_2C_4H_2O_4 \cdot 2H_2O$ and $2KHC_4H_2O_4 \cdot H_2C_4H_2O_4$, he must have recovered not only these two salts separately as he reports, but crystals of $KHC_4H_2O_4$ must also have been present. Rieckher's description (1) of crystals of the normal salt actually suggests $KHC_4H_2O_4$, while his varied comments on crystals of the latter sometimes suggest $2KHC_4H_2O_4 \cdot H_2C_4H_2O_4$. If the crystals which Repossi (8) employed for his optical crystallographic study of $KHC_4H_2O_4$ were recrystallized from water, without any adjustment of the pH of the solution, they may actually have been those of $2KHC_4H_2O_4 \cdot H_2C_4H_2O_4$.

UNIT CELL AND SPACE GROUP DATA

The unit cell constants and the space group of $KHC_4H_2O_4$ and of $K_2C_4H_2O_4 \cdot 2H_2O$ were determined by the Buerger precession method using $Mo K\alpha$ ($\lambda = 0.7107 \text{ \AA}$) radiation for the first and $Cu K\alpha$ ($\lambda = 1.5418 \text{ \AA}$) radiation for the second. Film shrinkage corrections were applied to all film measurements. Corresponding data for $2KHC_4H_2O_4 \cdot H_2C_4H_2O_4$ have been reported by Gupta (11) and, therefore, were not redetermined in the present

TABLE III
X-Ray diffraction powder data for $KHC_4H_2O_4$ (indexed for $d > 2.20 \text{ \AA}$)

$d \text{ (\AA)}$				$d \text{ (\AA)}$				$d \text{ (\AA)}$	
I/I_1	Obs.	Calc.	hkl	I/I_1	Obs.	Calc.	hkl	I/I_1	Obs.
13	6.866	6.866	010	—	—	2.666	120	2	1.915
10	5.940	5.945	100	—	—	2.644	220	8BB	1.854
1	5.541	5.523	101	15	2.585	2.590	022	15	1.786
15	5.272	5.288	110	—	—	2.568	002	1	1.759
—	—	5.181	011	25	2.524	2.528	111	10	1.739
—	—	5.135	001	—	—	2.517	221	8	1.703
—	—	4.669	111	—	—	2.485	210	8	1.671
20	3.991	4.012	111	15	2.470	2.475	031	1	1.626
—	—	3.976	110	—	—	2.467	112	15B	1.577
75	3.550	3.557	021	—	—	2.450	021	1	1.536
35	3.507	3.513	011	15	2.431	2.435	212	1	1.516
—	—	3.445	201	—	—	2.370	130	2BB	1.489
25	3.432	3.433	020	1	2.354	2.355	221	1	1.444
—	—	3.425	111	55	2.327	2.334	222	10	1.425
—	—	3.417	120	—	—	2.333	131	1	1.393
—	—	3.168	101	—	—	2.295	211	1	1.364
60	3.158	3.165	211	—	—	2.288	030	1	1.350
—	—	3.140	121	—	—	2.280	301	1BB	1.324
—	—	3.096	112	1	2.272	2.270	311	2	1.283
—	—	3.059	210	45	2.240	2.240	131	1	1.262
—	—	3.000	211	—	—	2.214	221	2	1.238
100	2.965	2.973	102	8	2.205	2.204	302	5	1.210
—	—	2.972	200, 121	—	—	—	—	5	1.194
—	—	2.783	012	5	2.144	—	—	2	1.184
20	2.774	2.761	202	1	2.116	—	—	1	1.164
—	—	2.733	121	5	2.084	—	—	1	1.142
—	—	2.710	212	1	2.048	—	—	1BB	1.142
15B	2.698	2.692	122	40	2.000	—	—	1BB	1.104
—	—	—	—	15B	1.961	—	—	—	—

investigation. Densities (at about 20° C) were measured by flotation in binary solutions of toluene and ethylene dibromide in the case of "acid" potassium hydrogen fumarate, and toluene and methylene iodide in the other two cases. Data for the three salts are summarized in Table I.

The unit cell of $2\text{KHC}_4\text{H}_2\text{O}_4 \cdot \text{H}_2\text{C}_4\text{H}_2\text{O}_4$ represented in Table I(A) was derived by Delaunay reduction from that of Gupta (11), $a = 8.64 \text{ \AA}$, $b = 7.48 \text{ \AA}$, $c = 6.96 \text{ \AA}$, $\alpha = 78.1^\circ$, $\beta = 112.9^\circ$, $\gamma = 107.9^\circ$, although the latter is the more convenient structurally. The transformation matrix from the original cell (1) to the reduced cell (Table I) is 010/101/00 $\bar{1}$.

In the case of $\text{KHC}_4\text{H}_2\text{O}_4$ the reciprocal lattice elements of two different cells were measured and both were reduced to that represented in Table I(B). The direct cell elements of the first were $a = 6.92_2 \text{ \AA}$, $b = 6.95_2 \text{ \AA}$, $c = 17.95_7 \text{ \AA}$, $\alpha = 36^\circ 44'$, $\beta = 32^\circ 11'$, $\gamma = 53^\circ 31'$; transformation matrix to give the reduced cell of Table I(B),

TABLE IV
X-Ray diffraction powder data for $\text{K}_2\text{C}_4\text{H}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$ (indexed for $d > 2.24 \text{ \AA}$)

$d \text{ (\AA)}$				$d \text{ (\AA)}$				$d \text{ (\AA)}$	
I/I_1	Obs.	Calc.	hkl	I/I_1	Obs.	Calc.	hkl	I/I_1	Obs.
30	9.152	9.114	020	100BB	2.810	2.824	042	20	2.088
—	—	6.693	011			2.814	151	25	2.047
40	6.295	6.287	100			2.801	122	1	2.028
5	5.952	5.943	110			2.799	061	1	2.004
40	5.636	5.647	021	—	—	2.792	230	75	1.982
15	5.180	5.175	120			2.735	160	1	1.956
2	4.929	4.926	11 $\bar{1}$			2.724	23 $\bar{1}$	2	1.929
—	—	4.642	031			2.708	211	1	1.903
30	4.558	4.557	040	75B	2.706	2.693	142	20B	1.890
1	4.461	4.461	12 $\bar{1}$			2.649	132	1	1.864
—	—	4.369	130			2.623	221	1	1.848
—	—	4.302	111			2.612	16 $\bar{1}$	15	1.822
35	3.987	3.982	121	—	—	2.588	240	25	1.798
25	3.905	3.913	13 $\bar{1}$			2.561	052	1	1.781
—	—	3.850	041			2.558	202	10	1.752
1	3.684	3.690	140			2.533	212, 24 $\bar{1}$	10B	1.636
30	3.581	3.598	002	5	2.532	2.505	161	8B	1.576
—	*	3.578	131			2.497	231	8B	1.552
—	—	3.530	012			2.473	142	1B	1.523
—	—	3.403	14 $\bar{1}$			2.463	222	1	1.487
80	3.342	3.346	022	30	2.471	2.462	152	20	1.474
—	—	3.338	102			2.448	071	1B	1.440
80	3.285	3.283	112			2.406	170	10	1.411
—	—	3.252	051			2.381	250	10	1.400
20B	3.156	3.175	141	2	2.382	2.378	013	2	1.384
		3.154	150			2.358	232	2	1.368
		3.143	200			2.347	241	2	1.353
		3.134	122			2.338	113, 25 $\bar{1}$	8	1.303
25	3.099	3.098	210	45	2.323	2.321	062, 17 $\bar{1}$	8	1.296
		3.096	032			2.319	023	15	1.282
		3.038	060			2.290	152	2	1.262
		3.005	211			2.282	123	2	1.250
30	3.012	2.972	220	45	2.281	2.278	080	2	1.224
45B	2.950	2.969	151			2.247	162	2B	1.202
		2.944	102			2.244	171	1	1.176
		2.926	132			2.150		1	1.130
		2.906	112	10	2.244				
5	2.900	2.890	221	15	2.198				
				1	2.120				

*Reflection probably present but with $I/I_1 < 1$.

010/ $\bar{2}$ 11/ $\bar{1}$ 0. The direct cell elements of the second were $a = 12.70$, \AA , $b = 13.13$, \AA , $c = 18.03$, \AA , $\alpha = 161^\circ 33'$, $\beta = 163^\circ 07'$, $\gamma = 27^\circ 56'$; transformation matrix to give the reduced cell of Table I(B), 110/ $\bar{1}$ 22/ $\bar{1}$ 01. Numerical values for corresponding reduced-cell constants agreed to better than 0.01 , \AA in linear dimensions, and $20'$ in the angles; the values selected for Table I(B) are those for the first cell because they gave slightly better agreement with the powder data.

POWDER IDENTIFICATION DATA

The powdered samples were taken up in thin-walled glass capillary tubes as described elsewhere (12), and cylindrical cameras of 114.6-mm diameter were employed. The photographs were taken with Co $K\alpha$ radiation ($\lambda = 1.790$ \AA), Straumanis film mounting, and the apparatus "cut-off" was about 20 \AA . Film shrinkage corrections were $<1/1000$, and were not applied to the measurements. Intensities were estimated visually with the aid of a calibrated strip. The patterns were indexed on the basis of the unit cell and space group data of Table I, with the exception of $2\text{KHC}_4\text{H}_2\text{O}_4 \cdot \text{H}_2\text{C}_4\text{H}_2\text{O}_4$ for which the constants of the unreduced cell (11) were employed. The results are given in Tables II, III, and IV, where B and BB in the columns of I/I_1 indicate lines which were broader and much broader, respectively, than the general average for a given pattern, and an asterisk in the columns of d (obs.) indicates that the reflection probably was present but with $I/I_1 < 1$, thus making a reasonably accurate measurement of 2θ impractical.

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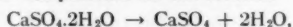
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ON THE SOLUBILITY OF ANHYDROUS CALCIUM SULPHATE AND
OF GYPSUM IN CONCENTRATED SOLUTIONS OF SODIUM CHLORIDE
AT 25° C, 30° C, 40° C, AND 50° C¹

E. BOCK

ABSTRACT

The solubilities of anhydrous CaSO_4 and $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ in concentrated aqueous solutions of NaCl at a series of temperatures—25° C, 30° C, 40° C, and 50° C, have been determined. It was found that the transition temperature for the reaction



which in pure water has a value of 42° C, is shifted progressively to lower temperatures with increasing NaCl concentration. It was also found that the variation of the transition temperature with NaCl concentration could be adequately represented by the equation

$$\Delta G = \Delta H - T\Delta S + 2RT \ln P/P_0,$$

where ΔG , ΔH , and ΔS are the Gibbs free energy, enthalpy, and entropy of the reaction and P_0 and P are the vapor pressures of pure water and the solution respectively at the absolute temperature T .

INTRODUCTION

It has long been known that the gypsum-anhydrite transition point is depressed by addition of strong electrolytes. However, it appears that no systematic study of this aspect of this system has ever been made, and only isolated experiments are reported in the literature (1).

Since many naturally occurring gypsum deposits which are used as raw material for the commercial production of plaster of paris and building plaster are contaminated with various amounts of sodium chloride, it was decided to carry out a systematic study of the behavior of the system gypsum-anhydrite in the presence of varying amounts of sodium chloride. The results of such a study should afford a clearer understanding of the factors that govern the deposition of anhydrite or gypsum, as the case may be, from a slurry of hemihydrate ($\text{CaSO}_4 \cdot \frac{1}{2}\text{H}_2\text{O}$) and water, contaminated with NaCl.

EXPERIMENTAL

The salts used in this research, i.e. CaSO_4 anhyd., $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$, and NaCl, were all Fisher certified reagents of high purity. No recrystallization of the salts was attempted since it was felt that nothing would be gained by it in view of the high initial purity of the materials. An ignition analysis of $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ showed a loss in weight equal to the theoretically expected value of 20.8%. The anhydrous CaSO_4 was heated at 900° C for 1 hour and subsequently kept in a desiccator at a temperature of 60° C.

Saturated solutions of gypsum and anhydrite were obtained as follows. Excess solid was added to an aqueous solution of sodium chloride of known composition. The latter was contained in an all-hard-pyrex-glass solubility cell (Fig. 1). The cell and contents were then immersed in a water bath the temperature of which was controlled by an electronic relay and was constant to within 0.05° C. The temperature of the water bath was read by means of a Beckmann thermometer. The latter was calibrated against a standard platinum resistance thermometer. The solutions were agitated for at least 48 hours by means of a pyrex-glass stirrer. This time interval was found to be quite

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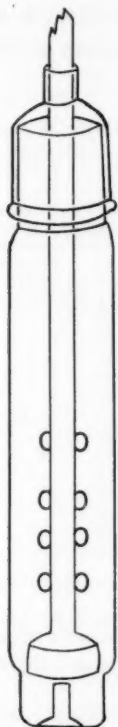


FIG. 1. Solubility cell.

satisfactory in the case of the more stable solid phase. Thus periodic checks in which the solution was stirred for 48 hours, 72 hours, and 96 hours showed no difference in the solubility, i.e. the solubility was identical within the limits of experimental error of $\frac{1}{2}\%$. In the case of the less stable solid phase some difficulties were encountered. It was found that the solubility decreased with longer periods of stirring. It was necessary to make several solubility determinations for different durations of stirring. The maximum solubility value was taken as the "true" solubility of the phase.

After it was deemed that the solution had been stirred for a sufficient length of time, the excess solid was separated from the liquid phase by quickly emptying the contents of the solubility cell into a large sintered-glass filter and applying suction to the suction flask by means of a water aspirator. The act of filtration never lasted longer than 1 minute, thus making any possible loss of water due to evaporation from the saturated solution negligible.

The analysis of the saturated solution was carried out as follows. Two 50-ml samples of the solution were put into two previously weighed Erlenmeyer flasks. The latter were immediately stoppered with rubber stoppers. The flasks and contents were weighed on an analytical balance. Next, the calcium ion concentration was determined by titration with standard E.D.T.A. using "Calred" as indicator. The sodium chloride content was similarly determined on two different samples by titration with standard AgNO_3 solution following Mohr's method. Blanks were run in each case.

EXPERIMENTAL RESULTS

The experimental results are summarized in Table I. In this table is recorded the solu-

TABLE I
Solubility of CaSO_4 and $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ in sodium chloride solutions

Moles of NaCl in 1000 g water	Solubility, g CaSO_4 /100 g water		Moles of NaCl in 1000 g water	Solubility, g CaSO_4 /100 g water	
	CaSO_4	$\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$		CaSO_4	$\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$
25° C			40° C		
—	0.275	0.207	—	0.225	0.218
1.00	0.751	0.614	0.94	0.630	0.607
1.59	0.816	0.709	1.77	0.691	0.720
2.58	0.831	0.773	2.90	0.697	0.760
3.70	0.770	0.741	3.70	0.640	0.736
4.67	0.664	0.698	4.70	0.572	0.690
5.24	0.631	0.647	5.60	0.508	0.632
30° C			50° C		
—	0.262	0.222	—	0.190	0.212
0.92	0.688	0.600	0.93	0.522	0.599
1.72	0.764	0.713	1.80	0.611	0.722
2.85	0.768	0.755	2.88	0.619	0.775
3.70	0.720	0.726	3.70	0.590	0.752
4.64	0.635	0.658	4.71	0.521	0.700
5.55	0.564	0.616	6.30	0.486	
			5.87		0.638

bilities of gypsum and anhydrite at various temperatures and sodium chloride concentrations. In Figs. 3 and 4 the solubilities are represented in a graphical manner. Figure 3

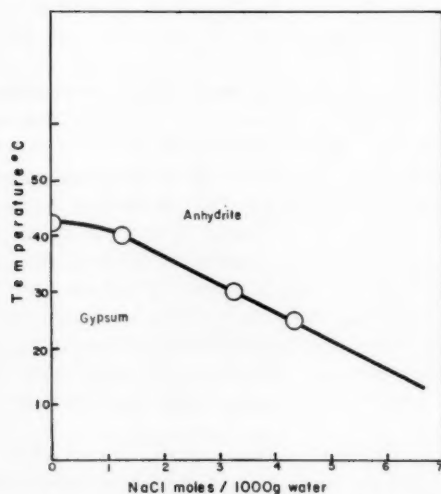


FIG. 2. Variation of transition point with temperature.

shows the solubilities of the two salts in pure water. Lastly, Fig. 2 shows the variation of the transition-point temperature with sodium chloride content of the solution.

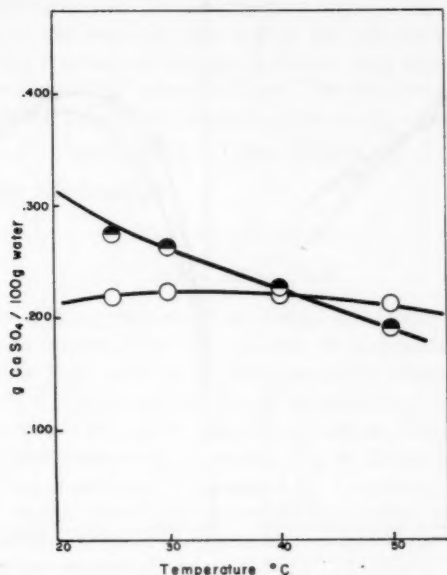


FIG. 3. Solubility in pure water: \bullet CaSO_4 anhyd., \circ $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$.

DISCUSSION OF RESULTS

From the phase rule it is known that the number of degrees of freedom F , i.e. the number of undetermined variables of a system consisting of C components which are in mutual equilibrium and exist in P phases, is given by the expression

$$F = C - P + 2. \quad [1]$$

An aqueous solution of gypsum or anhydrite, containing, in addition, dissolved sodium chloride, constitutes a system of three components: CaSO_4 , NaCl , and H_2O . If the temperature and pressure are fixed at some arbitrary value, the vapor phase may be disregarded. Hence if all sodium chloride is in solution there are only two phases present: the liquid phase—solution, and the solid phase— CaSO_4 anhyd. or $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$. From eq. [1] it is apparent that F , the number of degrees of freedom, is unity. However, as soon as a second solid phase appears, the system will become invariant, i.e. $F = 0$. It is clear that when $F = 0$ the solution must be saturated with respect to both solid phases, CaSO_4 anhyd. and $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$. In other words, the two solids will be in equilibrium with one another. By determining the solubility of both salts separately and constructing a plot of solubility versus sodium chloride content of solution, it is possible from the intersection of the two corresponding isotherms to obtain the transition-point temperature of the two salts. That is, the point of intersection of the two curves represents that state of affairs in which both salts have the same solubility and this, as has been shown above, is just the condition for equilibrium. Hence the temperature of the isotherm is the transition temperature for the system in the presence of a certain definite quantity of sodium chloride, the actual quantity of which is defined by the intersection of the two isotherms. By plotting the temperature of the isotherms versus the sodium chloride

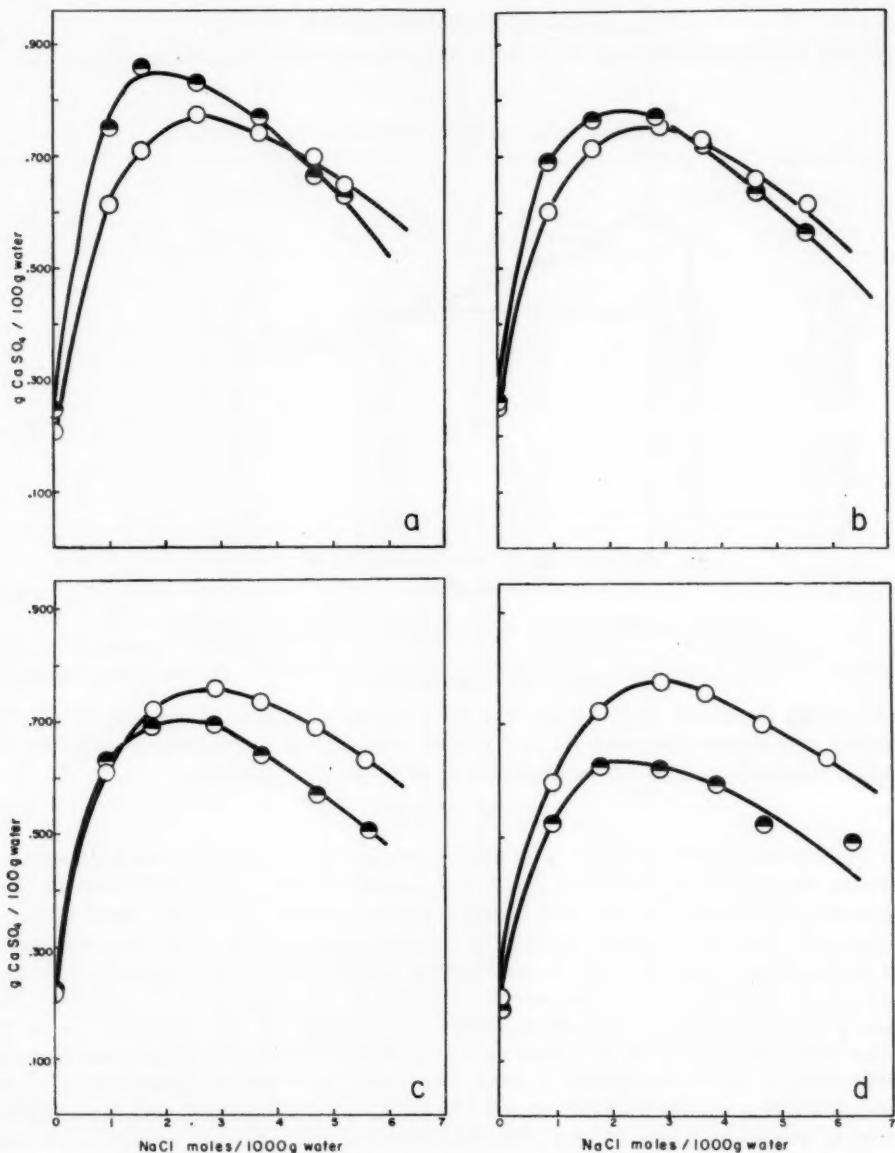


Fig. 4. Isotherms: (a) 25° C, (b) 30° C, (c) 40° C, (d) 50° C; ● CaSO₄ anhyd., ○ CaSO₄·2H₂O.

content of the solutions corresponding to the intersection points a graph is obtained which represents the variation of the transition-point temperature with sodium chloride content of solution. By means of this graph (Fig. 2) one can predict the nature of the precipitate that will result from an evaporation of a solution of CaSO₄ containing a known quantity of sodium chloride. Thus, for all solutions of a given sodium chloride content, CaSO₄

anhyd. will be deposited provided the temperature is above the curve in Fig. 2 or, alternatively, gypsum will be the solid thrown out if the temperature is below the curve.

The variation of the transition-point temperature with sodium chloride content may be also derived from theoretical considerations. The problem is to derive an expression for the variation of the equilibrium constant with temperature for the reaction



Employing the known relationships

$$\Delta G^0 = -RT \ln K, \quad [3]$$

$$\Delta G^0 = \Delta H^0 - T\Delta S^0, \quad [4]$$

where ΔG^0 , ΔH^0 , and ΔS^0 are the standard Gibbs free energy, enthalpy, and entropy and K the equilibrium constant for the reaction, it is possible to arrive at a value of K for any temperature T provided the other quantities involved are known. This procedure was employed by Macdonald (2) in the calculation of the transition point for the above system. A few words should be said concerning the water term on the right-hand side of eq. [2]. This term refers to pure water. But in presence of NaCl the water is no longer pure; its activity is said to be depressed by the presence of NaCl. The extent of this depression may be calculated approximately from vapor pressure values of aqueous sodium chloride solution. These are extensively recorded in the *International Critical Tables* (3). Inserting the numerical values for ΔH , ΔS ; and R the gas constant (4), and recognizing that at equilibrium, $\Delta G = 0$, one obtains

$$\Delta G = 163.89T + 0.0215T^2 - 65.17 \log_{10} T - 2495 + 2RT \times 2.303 \log_{10} (P/P_0). \quad [5]$$

Table II shows a number of calculated transition-point temperatures along with those

TABLE II
Variation of transition point with temperature

Moles of NaCl in 1000 g water	Temperature, °C	
	Experimental	Calculated
5.30	20.0*	19.0
4.30	25.0	25.2
3.28	30.0	31.0
2.30	35.0	32.5
0.00	42.0	40.0

* Extrapolated.

experimentally determined. The agreement is quite satisfactory if one takes into account the approximations involved in arriving at eq. [5].

ACKNOWLEDGMENT

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THE RELATIVE BASICITIES OF WATER, METHANOL, AND ETHANOL¹

C. E. NEWALL AND A. M. EASTHAM

ABSTRACT

From the kinetics of the reaction of ethylene oxide with aqueous ethanol and methanol, catalyzed by perchloric acid, the relative basicities of water, methanol, and ethanol have been determined. The value of K_1 in the expression

$$K_1 = \frac{[\text{H}_3\text{O}^+][\text{ROH}]}{[\text{H}_2\text{O}][\text{ROH}_2^+]}$$

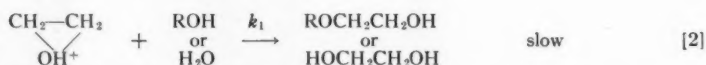
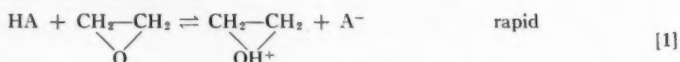
has been found to be 1.2×10^3 for methanol and 2.1×10^3 for ethanol, in good agreement with previous values.

In alcohol solution a number of acid-catalyzed reactions are known to be strongly retarded by traces of water (1, 2, 3). The generally accepted explanation of this effect, first put forward by Goldschmidt about 1900 (2), attributes the decrease in rate to the great affinity of water for protons, with a resulting conversion of the acid ROH_2^+ to the weaker H_3O^+ . This view has received strong support in recent years from measurements of the relative basicity of water with respect to alcohols, notably by Braude and Stern (4), Koskikallio (5), and others (6). The results indicate that K_1 , where

$$K_1 = \frac{[\text{H}_3\text{O}^+][\text{ROH}]}{[\text{ROH}_2^+][\text{H}_2\text{O}]},$$

has a value of about 100 for methanol and 200 for ethanol at ordinary temperatures.

Our studies of the acid-catalyzed reaction of ethylene oxide with alcohols have prompted us to attempt an estimation of K_1 for methanol and ethanol from kinetic data. This reaction seems particularly well suited to the purpose not only because it shows a large and easily measured retardation by water, but because the uncatalyzed reaction is negligibly slow, and because it now seems quite certain that the reaction mechanism involves a preliminary rapid proton transfer to equilibrium, followed by a slow reaction of the protonated epoxide with the solvent.



Furthermore, water and alcohols react at rather similar rates with the protonated epoxide so at low water concentrations the value of k_1 can be assumed to be independent of the solvent over a workable range of solvent compositions.

From the equilibrium expressions

$$K_2 = \frac{[\text{oxide.H}^+][\text{ROH}]}{[\text{oxide}][\text{ROH}_2^+]} \quad \text{and} \quad K_3 = \frac{[\text{oxide.H}^+][\text{H}_2\text{O}]}{[\text{oxide}][\text{H}_3\text{O}^+]} = K_2/K_1$$

and from the reasonable approximations: (a) that the sum of the concentrations of ROH_2^+ and H_3O^+ equals the concentration of added acid (i.e. that ionization is complete and the concentration of protonated epoxide very small), and (b) that $[\text{H}_3\text{O}^+]$ is small

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compared to [H₂O], one can derive, as the rate expression for the reaction at low water concentrations, the equation

$$-d(\text{oxide})/dt = k_1 K_2 [\text{HA}][\text{oxide}] \left\{ \frac{[\text{ROH}]}{K_1 [\text{H}_2\text{O}] + [\text{ROH}]} \right\} \quad [3]$$

which in anhydrous solution reduces to the usual rate expression

$$-d(\text{oxide})/dt = k_1 K_2 [\text{HA}][\text{oxide}].$$

K_1 can then be estimated either by measuring $k_1 K_2$ in anhydrous alcohol and solving equation [3] at various water concentrations or by plotting $1/k_{\text{sp}}$ against [H₂O], where

$$k_{\text{sp}} = \frac{-d(\text{oxide})/dt}{[\text{HA}][\text{oxide}]} = \frac{k_1 K_2 [\text{ROH}]}{K_1 [\text{H}_2\text{O}] + [\text{ROH}]}, \quad [4]$$

$$1/k_{\text{sp}} = \frac{K_1 [\text{H}_2\text{O}]}{k_1 K_2 [\text{ROH}]} + \frac{1}{k_1 K_2}.$$

Since, at low water concentrations, [ROH] is approximately constant, the plot is a straight line of slope $K_1/k_1 K_2 [\text{ROH}]$ and intercept $1/k_1 K_2$.

EXPERIMENTAL

Rate measurements were made dilatometrically, evaluated by the Guggenheim method (7), and expressed in terms of moles per liter per minute at 25° C, essentially as previously described (3). Ethylene oxide was measured out as the vapor in a vacuum system and sealed into ampoules which were then broken into the reaction mixture. Methanol was dried with magnesium turnings in the usual way and used to dilute a stock solution of perchloric acid in dry methanol. The stock solution was prepared from the commercial 70% acid (HClO₄·2H₂O). For a few experiments in which an attempt was made to reduce the water content below the 0.01 *M* limit imposed by the 70% acid, anhydrous perchloric acid was prepared in the vacuum apparatus as described elsewhere (8) and diluted at low temperature with dry methanol.

Data for ethanol were taken from the previous paper (3).

RESULTS

The average values of k_{sp} for a series of mixtures of methanol and water are shown in Table I.

TABLE I

[H ₂ O]	[CH ₃ OH]	k_{sp} (av.) (l. mole ⁻¹ min ⁻¹)	Glycol in product (mole%)	H ₂ O in solvent (mole%)
55.6	—	0.58	101	100
50	2.5	0.61	92	95
40	6.5	0.51	77.5	86
30	11	0.48	63	73
20	15	0.345	50	57
12	19	0.35	34	39
8	20	0.39	26	29
4	22	0.73	17	15
2	24	1.35	10	7.7
1	24	2.3	(5)	4
0.50	24.5	4.1	(4)	2
0.25	24.5	5.7		
0.10	24.5	10.4		
0.02	24.5	13.7		
0.01	24.5	12.5		
0.0	24.5	14.1		

It is apparent from the product analysis that, over most of the range of solvent mixtures, methanol is somewhat more reactive than water. The deviations at low water concentrations are believed to be due to experimental errors in determining the small amounts of glycol present, errors resulting from some oxidation of the methanol. Certainly there is no indication in the analyses that k_1 cannot be considered constant over small changes in solvent composition.

Attempts to determine k_1K_2 by direct measurement of the rate in anhydrous methanol were not very successful, apparently because the reaction is so sensitive to traces of water. Improved techniques could doubtless reduce the error but as the final results show that an error of 1% in the rate corresponds to an error of less than 0.002 *M* in the concentration of water, this approach does not appear very promising. The best values of k_1K_2 appear to be those obtained by extrapolating the plot of $1/k_{sp}$ against $[H_2O]$ to zero water concentration (Fig. 1). The plots are linear up to 1–2 *M* water and yield the following constants:

	Methanol	Ethanol
k_1K_2	13.7	6.7
K_1	1.2×10^3	2.1×10^3

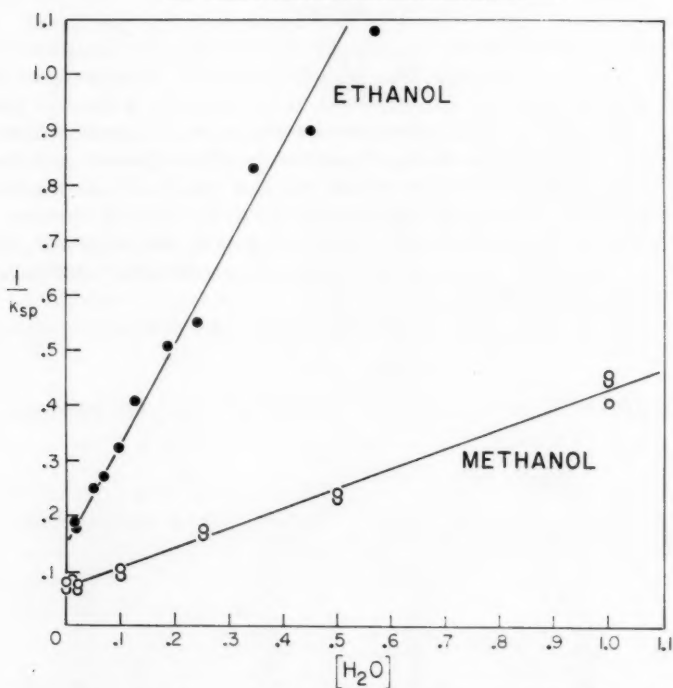


FIG. 1. Plots of $1/k_{sp}$ against water concentration: ● in ethanol (data of Brown and Eastham (3)); ○ in methanol.

The value of K_1 for ethanol is in good agreement with the value of 220 obtained by Braude and Stern (4) from indicator measurements, presumably at about 20° C, while the value for methanol is consistent with values from 110 to 140 obtained by various workers and by a variety of methods, at 25° (5).

While the agreement of the present values of K_1 with other work seems good, inspection of the data suggests that the probable error in our values may be as high as $\pm 10\%$. The error lies largely in the value for k_1K_2 since the extrapolation is by no means precise. There is, however, one rather disturbing feature of the results, namely the relative values of k_1K_2 for the two alcohols. If K_1 is twice as large for ethanol as for methanol then one might expect the same to be true for K_2 , and it follows that k_1 should be about four times as large for methanol as for ethanol. The glycol analyses, however, suggest that k_1 cannot be more than twice as large for methanol as for ethanol. A comparison of this kind is perhaps dangerous since the two sets of constants were obtained in different solvents (methanol and ethanol) but does suggest that the results should be treated with caution.

In Fig. 2, values of k_{sp} calculated from the above constants have been plotted, along

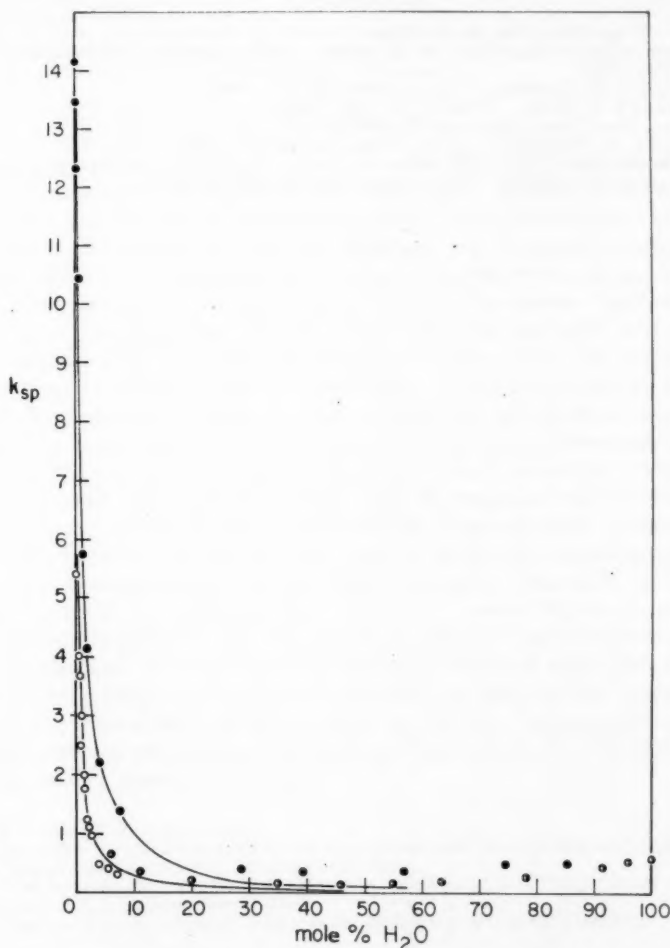


FIG. 2. Plots of k_{sp} against solvent composition. Solid lines are rates calculated for methanol and ethanol from the values of k_1K_2 and K_1 obtained in this work. Circles are experimental values: ● methanol-water; ○ ethanol-water; ◐ ethanol-water at constant ionic strength ($\text{ClO}_4^- = 0.055 M$).

with the experimental data, against the solvent composition. As the proportion of water in the solvent increases, deviations from the calculated rates become severe at about 10–15 mole% water, while at about 50 mole% water the rate starts to increase again. These changes may be due in part to general medium effects such as changes in the dielectric constant but there are also a number of specific causes which have not been taken into account here. In particular we may note (a) that salt effects are about five times larger in ethanol than in water so a small rate decrease should occur with increasing water, (b) that equation [3] treats the solvent as pure alcohol and does not allow for an increase in molarity (from 17 to 55 in the case of ethanol–water) as the water concentration increases, and (c) over a wide range of concentrations the value of k_1 will not be constant in methanol–water mixtures because of the lower reactivity of water.

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CORRELATIONS OF INFRARED GROUP FREQUENCIES AND BAND INTENSITIES IN ORGANIC MOLECULES WITH SUBSTITUENT CONSTANTS: A STATISTICAL EVALUATION¹

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ABSTRACT

A statistical evaluation of the empirical linear correlations of infrared group frequencies and band intensities in aliphatic and benzene derivatives with substituent constants has been carried out. The correlations of frequencies with substituent constants generally give low standard deviations and acceptable correlation coefficients, and may thus be employed for the estimation of substituent constants. The correlations of band intensities with substituent constants show an interesting trend of the sign and magnitude of the slopes (ρ values) with the electrical property of the bond or group involved in the vibration. The ρ value decreases with the increasing electron-withdrawing power of the group.

INTRODUCTION

Although the various substituent constants were devised to correlate the structure of organic molecules with their chemical reactivity, many physical properties of the molecules may also be correlated with these constants (1, 2). Such empirical or semiempirical relations give a better insight into the structure and behavior of organic molecules, particularly when the chemist cannot yet disentangle the various structural factors into finer and more fundamental contributions. Considerable interest has been exhibited, in recent years, in correlating the infrared group frequencies and band intensities of related groups of organic molecules with substituent constants (3-9). The infrared frequencies and intensities are controlled by different factors. While the frequency is mainly determined by the bond force constants, the intensity is controlled by dipole derivatives with respect to bond length, $(\delta\mu/\delta r_{ij})$. Change of substituent group may affect the force constants, static dipole moments, or $(\delta\mu/\delta r_{ij})$, through inductive or (and) resonance effects. Substituent groups generally affect both the frequency and the intensity, though not always in the same direction. Sometimes the frequency shift is very small and the change in band intensity is large or vice versa. It is therefore important to correlate the frequencies and intensities of groups with substituent constants to understand the mechanism(s) involved. Although there have been several reports of such correlations with substituent constants in the literature (3-9), there has been no systematic evaluation of these correlations. We have now carried out a statistical evaluation (10) of the correlations of group frequencies and band intensities of aliphatic and benzene derivatives, in order to test the validity and utility of the correlations. Such an evaluation is justified by the high precision and accuracy of the recent infrared data on related groups of organic molecules, used in these correlations.

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RESULTS AND DISCUSSION

A linear relation of the infrared group frequencies in meta- and para-disubstituted benzene derivatives with the Hammett σ constants (11) has been suggested by several workers (3, 8, 12). The relation may be expressed by a Hammett-type equation,

$$[1] \quad \nu = \nu_0 + \rho\sigma,$$

where ν is the observed group frequency in the meta- or para-disubstituted benzene, ν_0 is the group frequency in the monosubstituted derivative, and σ and ρ have their usual significance. Thompson *et al.* (3) have expressed doubt about the roughly linear plots of ν against σ having much significance and have considered the possibility of plotting ν^2 versus σ . A linear relationship of the group frequencies in the meta- and para-benzene derivatives has also been proposed (4) with the electrophilic substituent constants, σ^+ (13, 14).

$$[2] \quad \nu = \nu_0^+ + \rho^+\sigma^+$$

The σ^+ values differ from the σ values by an extra resonance factor resulting from greater opportunity for resonance in electrophilic reactions. The results of the statistical treatment of the correlations of the available data on the infrared group frequencies of benzene derivatives, with the σ and σ^+ constants, have been summarized in Table I. The σ constants were taken from the recent compilation by McDaniel and Brown (27) and σ^+ constants from the compilations by Brown and Okamoto (14). For the 18 sets of frequencies of meta- and para-substituted benzene derivatives correlated with the σ and σ^+ constants, the average standard deviations for the ν - σ and ν - σ^+ correlations are 3.3 and 3.3 cm^{-1} respectively, while the correlation coefficients are 0.938 and 0.924 respectively. It may be concluded that both the substituent constants correlate the frequencies equally well. This is not completely unexpected, because the vibrational frequencies, being associated with mechanical properties of bonds, may not show any preference between σ and σ^+ constants.

A linear relationship of the infrared group frequencies in aliphatic derivatives with the σ^* constants of Taft (28) has been proposed.

$$[3] \quad \nu = \nu_0^* + \rho^*\sigma^*$$

The results of the statistical evaluation of the correlations of the available data with the σ^* constants have been summarized in Table II. The average standard deviation is rather high (14.1 cm^{-1}), compared to the value of 3 cm^{-1} in the case of benzene derivatives (Table I).

Several possible correlations of infrared band intensities in meta- and para-substituted benzene derivatives with σ and σ^+ constants have been suggested (3, 4, 5, 9, 36). The best correlation is probably between the logarithm of the vibrational band intensities, $\log A$, and the substituent constants. Thompson and co-workers (3, 8) have correlated $\log A$ with Hammett σ constants:

$$[4] \quad \log A = \log A_0 + \rho\sigma.$$

Rao (4, 9, 22) has suggested a similar linear relation with the σ^+ constants:

$$[5] \quad \log A = \log A_0^+ + \rho^+\sigma^+.$$

TABLE I
Correlation of infrared group frequencies in *p*- and *m*-substituted benzene derivatives with σ and σ^+ substituent constants

Series	Solvent	Frequency	ν_0^b (cm ⁻¹)	ρ^c	s^d	r^e	ν_0^{+b} (cm ⁻¹)	ρ^{+c}	s^d	r^e	n^f
Phenols (15) ^a	C	POH	3610	-13.4	5.3	0.958	3608	-9.51	3.3	0.924	15, 14
Benzoic acids (16)	C	POH	3553	-10.1	3.4	0.793	3552	-10.6	2.4	0.956	6
Benzoyl peroxides (17)	D	PC=O	1776	18.3	3.3	0.978	1779	12.5	4.1	0.898	10
Benzophenones (12)	C	PC=O	1663	13.9	1.5	0.946	1664	6.9	3.6	0.831	9
Acetophenones (18)	C	PC=O	1690	15.9	1.6	0.975	1692	10.6	3.3	0.974	14
Benzaldehydes (3)	C	PC=O	1704	10.9	2.8	0.872	1707	9.1	3.1	0.989	7, 6
Benzoic acids (16)	C	PC=O (monomer)	1742	12.9	1.5	0.962	1743	9.1	2.0	0.961	6
Benzoic acids (16)	C	PC=O (dimer)	1695	14.2	3.1	0.994	1697	9.9	1.4	0.976	6
Ethyl benzoates (3)	C	PC=O	1717	14.9	2.9	0.959	1719	9.9	1.7	0.977	6
Acetanilides (8)	CH	PC=O	1691	21.1	3.3	0.940	1694	13.9	1.3	0.904	8
Acetanilides (19)	C	PNH(trans)	3437	-3.0	2.8	0.835	3436	-1.8	2.3	0.783	10, 9
Anilines (20) ^a	C	PNH(asym)	3476	30.5	3.8	0.979	3482	21.3	4.0	0.864	16
Anilines (21) ^a	C	PNH(asym overtone)	—	—	—	—	6697	41.3	2.9	0.992	19
Anisoles (22)	C	PC-O-C	1243	14.6	5.1	0.868	1246	14.5	5.7	0.782	10
Nitrobenzenes (23)	B	PNO ₂ (asym)	1523	30.5	3.6	0.961	1528	19.2	5.6	0.934	9
Benzonitriles (24)	C	PC≡N	2232	7.4	1.4	0.965	2233	5.3	3.6	0.954	9
Isothiocyanates (25)	C	PN=C=S	2048	-48.2	6.0	0.987	2042	-30.0	5.9	0.981	7, 6
Thiocyanates (26)	CH	PG-C≡N	2167	8.3	5.1	0.977	2169	5.1	2.9	0.949	7
Av. 3.3											0.924

Note: solvents: C, carbon tetrachloride; D, dichloroethane; CH, chloroform; B, bromoform.

^aIn these systems σ^+ values ("dual" values) were used for some of the electron-withdrawing groups.

^bIntercept (value for the unsubstituted compound).

^cSlope.

^dStandard deviation in cm⁻¹.

^eCorrelation coefficient.

^fNumber of compounds in the correlation.

A statistical evaluation of the correlations of $\log A$ with σ and σ^+ constants (Table III) seems to indicate that σ^+ constants are probably better suited for the correlations. In some cases, like benzonitriles and anilines, the correlations with σ^+ constants are far superior. Such a preference to σ^+ constants is understandable, since band intensities are related to electrical properties of bonds. Excellent linear correlations have also been

TABLE II
Correlation of infrared group frequencies in aliphatic derivatives with Taft σ^* constants

Series	Solvent	Frequency	$\nu_0^*{}^a$	$\rho^*{}^b$	s^c	r^d	n^e
Simple aliphatic ketones (29)	C	$\nu_{C=O}$	1714	19.6	9.9	0.906	9
Hetero-atom conjugated ketones (30)	P	$\nu_{C=O}$	1654	53.8	17.3	0.954	6
Amides (31)	CH	$\nu_{C=O}$	1685	19.9	12.1	0.901	7
Acids (32)	C	ν_{OH}	3530	-9.4	0.5	0.995	11
Nitro compounds (33, 34)	C	$\nu_{NO_2}(\text{asym})$	1557	25.1	5.7	0.989	7
Simple and β -substituted nitriles (35)	CH	$\nu_{C\equiv N}$	2253	14.7	38.8	0.889	8
					Av.	14.1	0.939

NOTE: solvents: C, carbon tetrachloride; P, condensed phase; CH, chloroform.

^aIntercept (value for the unsubstituted compound).

^bSlope.

^cStandard deviation in cm^{-1} .

^dCorrelation coefficient.

^eNumber of compounds used in the correlation.

found between the logarithms of molar extinction coefficients, $\log \epsilon$, and σ^+ constants in the case of C—O—C stretching vibrations of anisoles (22) and NH stretching overtones of anilines (21).

The infrared band intensities in aliphatic derivatives may be correlated with σ^* constants:

$$[6] \quad \log A = \log A_0^* + \rho^* \sigma^*,$$

but the correlations are not satisfactory (Table IV).

GENERALIZATIONS

In the correlations of group frequencies with substituent constants, there is no particular relation between the sign and the magnitude of ρ and the nature of the bond or group involved in the vibration as might be expected. However, in the correlations of band intensities, there is a systematic variation of the sign of ρ with the nature of the bond involved. A negative slope of the $\log A - \sigma$, $\log A - \sigma^+$, or $\log A - \sigma^*$ plot is always found when the bond or the group involved is electron-withdrawing in nature, as in carbonyl derivatives and nitriles. A positive slope is found when the bond or group involved is electron-donating in character. The magnitude of ρ seems to vary in proportion to the extent to which the groups can withdraw or donate electrons. The slope of the $\log A - \sigma$ or $\log A - \sigma^+$ plot decreases with the increasing electron-withdrawing power of the group. These generalizations may be clearly seen from Table V.

This relation of the sign of ρ in the $\log A - \sigma$, $\log A - \sigma^+$, or $\log A - \sigma^*$ plot to the electrical property of the bond or group is found because the band intensity is itself dependent

TABLE III
Correlation of infrared band intensities in *m*- and *p*-substituted benzene derivatives with σ and σ^+ constants

Series	Solvent	Frequency	$\log A_0^a$	ρ^b	s^c	r^d	$\log A_0^{+e}$	ρ^{+f}	s^c	r^d	n^g
Benzaldehydes (3)	C	$\nu_{C=O}$	1.044	-0.089	0.021	0.916	1.040	-0.067	-0.068	0.986	5
Ethyl benzoates (3)	C	$\nu_{C=O}$	1.193	-0.080	0.023	0.945	1.205	-0.055	0.062	0.955	6
Acetanilides (8)	C	$\nu_{C=O}$	1.195	-0.145	0.033	0.979	1.173	-0.099	0.020	0.969	8
Phenols ^h (15)	C	ν_{OH}	0.790	0.137	0.040	0.879	0.813	0.106	0.040	0.875	14
Anilines ⁱ (20)	C	$\nu_{NH(asym)}$	1.188	0.166	0.053	0.889	1.217	0.130	0.044	0.923	16
Benzonitriles (36)	C	$\nu_{C\equiv N}$	0.356	-0.787	0.088	0.930	0.299	-0.461	0.033	0.982	7
					Av. 0.043	0.923			Av. 0.044	0.948	

NOTE: solvent: C, carbon tetrachloride.

^aIntercept (value for the unsubstituted compound).

^bSlope.

^cStandard deviation in cm^{-1} .

^dCorrelation coefficient.

^eNumber of compounds in the correlation.

^fIn these systems σ^- values ("dual" values) were used for some of the electron-withdrawing groups.

TABLE IV
Correlation of infrared band intensities in aliphatic derivatives with Taft σ^* constants

Series	Solvent	Frequency	$\log A_0^{*a}$	ρ^{*b}	s^c	r^d	n^e
Amides (31)	CH	$\nu_{C=O}$	0.613	-0.017	0.030	0.593	7
Alcohols (37)	C	ν_{OH}	0.681	0.397	0.082	0.881	12
Nitriles (35)	CH	$\nu_{C\equiv N}$	0.736	-0.491	0.087	0.792	8
					Av. 0.066	0.755	

NOTE: solvents: C, carbon tetrachloride; CH, chloroform.

^aIntercept (value for the unsubstituted compound).

^bSlope.

^cStandard deviation in cm^{-1} .

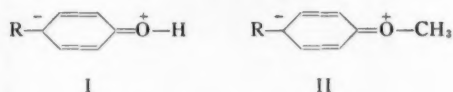
^dCorrelation coefficient.

^eNumber of compounds in the correlation.

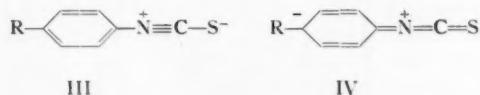
TABLE V
Generalizations regarding the correlation of infrared spectra of organic molecules with substituent constants

Series	Frequency	Group	para- σ of the group	$\log A - \sigma$ ρ	$\log A - \sigma^+$ ρ^+
Anilines (20)	ν_{NH}	$-\text{NH}_2$	-0.66	0.166	0.130
Phenols (15)	ν_{OH}	$-\text{OH}$	-0.37	0.137	0.106
Ethyl benzoates (3)	$\nu_{C=O}$	$-\text{COOC}_2\text{H}_5$	0.45	-0.08	-0.055
Nitriles (24)	$\nu_{C\equiv N}$	$-\text{CN}$	0.66	-0.26	-0.509

on $(\delta\mu/\delta r_{ij})$. Substituents favoring a dipole of a bond always increase its band intensity. Thus, the OH band intensity in phenols increases with electron-withdrawing ability of the group in the para or meta position (positive slope), while the $\text{C}\equiv\text{N}$ band intensity in benzonitriles increases with the increasing electron-donating ability of the para or meta substituent (negative slope). This type of generalization is extremely useful in identifying the prominent resonance forms in aromatic systems. For example, the most prominent resonance structures in phenols (I) and anisoles (II) should be similar since



the slopes of the $\log A - \sigma$ plots are positive in both cases (22). The most prominent resonance structure of the organic isothiocyanates has been proposed to be III (38) or IV (39). This proposal may now be supported by the band intensity measurements of Caldw



and Thompson (26) in para- and meta-substituted phenyl isothiocyanates. The $-\text{NCS}$ band intensity increases with the electron-withdrawing power of the substituents.

UTILITY OF THE CORRELATIONS IN ESTIMATING REACTIVITIES OF GROUPS

An obvious application of these different linear relations would be in the estimation of substituent constants of groups. The frequency correlation would be more useful for this purpose because frequencies can be measured very easily with high precision and accuracy. The measurement of band intensities, on the other hand, is rather tedious. One could, however, make use of extinction coefficient data, to a certain extent. If one were to employ the frequency correlations (Tables I and II) for estimating the substituent constant for a group, one has to determine the characteristic frequency of a functional group in the unsubstituted and substituted derivatives and then calculate the substituent constant by making use of the ρ values given in the tables (employing the same solvent). One should choose a functional group which has the most structure-sensitive frequency. Carbonyl stretching vibration is probably best for the purpose.

NOTE ADDED IN PROOF: Brown (40) has recently suggested that the substituent constants should be linearly related to the square roots of the infrared absorption intensities in substituted benzene derivatives. We have now carried out the statistical evaluation of the linear relations of $A^{1/2}$ with σ and σ^+ constants and have found that the $A^{1/2}-\sigma^+$ correlations are as good as the $\log A-\sigma^+$ correlations. The average standard deviation and correlation coefficient of $A^{1/2}-\sigma^+$ correlations for the six series of benzene derivatives (Table III) are found to be 0.081 and 0.957 respectively.

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THE PREPARATION OF SOME MERCAPTO MONOSACCHARIDES¹

N. C. JAMIESON AND R. K. BROWN

ABSTRACT

Methyl 4,6-O-benzylidene-2-benzylthio-2-deoxy- α -D-altropyranoside and methyl 4,6-O-benzylidene-3-benzylthio-3-deoxy- α -D-altropyranoside have been prepared by the reaction of sodium benzylmercaptide with methyl 2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside and methyl 2,3-anhydro-4,6-O-benzylidene- α -D-mannopyranoside respectively.

These two thio ethers were successfully reduced by sodium in liquid ammonia to methyl 2-deoxy-2-mercapto- α -D-altropyranoside and methyl 3-deoxy-3-mercapto- α -D-altropyranoside. An attempted replacement of the tosyl group in 1,2;5,6-di-O-isopropylidene-3-O-tosyl- α -D-glucufuranose by benzyl mercaptan was unsuccessful.

INTRODUCTION

The preparation of monosaccharides in which an oxygen atom has been replaced by a sulphur atom has received renewed attention in recent years, primarily due to the fact that these compounds provide a route to the synthesis of deoxy sugars. A review by Raymond covering the literature on thio sugars to 1944 (1) refers to the preparation of a number of thioglycosides and ω -deoxy- ω -alkylthio-hexoses and -pentoses. The only monosaccharide mentioned which contained a free mercapto group on a carbon atom other than the anomeric carbon (2-4) was a substance described as "3-deoxy-3-mercapto-D-glucose" obtained by Freudenberg and Wolf (5) in their attempt to apply the Tschugaeff reaction (6) to the preparation of an unsaturated monosaccharide.

Since 1944, a considerable amount of work has appeared in this area, but primarily concerning the preparation of the thioglycosides and thio ethers of monosaccharides (7-12). A few reports have been made of the preparation of monosaccharides with a free mercapto group. An improved synthesis of 1-thio-D-glucose by the reaction of hydrogen sulphide with 1,2-anhydro-D-glucose and its 3,4,6-tri-O-acetate in dimethylformamide has been described (13). The reduction with lithium aluminum hydride of 5,6-dideoxy-5,6-epithio-1,2-O-isopropylidene- β -L-idose has yielded 5,6-dideoxy-5-mercapto-L-idose (14). There has also been reported the preparation of 5,6-dideoxy-1,2-O-isopropylidene-5,6-(thiocarbonyldithio)- β -L-idose, a compound which, no doubt, can be reduced readily to 5,6-dideoxy-1,2-O-isopropylidene-5,6-dimercapto- β -L-idose with lithium aluminum hydride in accordance with similar reductions carried out on the trithiocarbonates of some hexitols (14, 15).

Since a number of mercapto monosaccharides were required in this laboratory, a program for their preparation was begun. This paper presents some results obtained in this direction.

RESULTS AND DISCUSSION

The debenzylation of S-benzylcysteine has been accomplished by the use of sodium in liquid ammonia (16) and this technique has been successfully applied in this laboratory to the preparation of mercaptoindoles (17). These results suggested that mercapto monosaccharides might be prepared by the reaction of benzyl mercaptan with suitable anhydro monosaccharides followed by the reductive cleavage of the resulting benzylthio ethers with sodium in liquid ammonia. This did indeed prove to be the case.

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Contribution from the Department of Chemistry, University of Alberta, Edmonton, Alberta. Taken from the thesis of N. C. Jamieson to be submitted to the Graduate School of the University of Alberta in partial fulfillment of the requirements for the degree of Master of Science.

When methyl 2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside (18, 19) was treated with sodium benzylmercaptide in methanol as solvent an almost quantitative yield of crystalline methyl 4,6-O-benzylidene-2-benzylthio-2-deoxy- α -D-altropyranoside was obtained. Similarly, methyl 2,3-anhydro-4,6-O-benzylidene- α -D-mannopyranoside (19), when treated with sodium benzylmercaptide, gave crystalline methyl 4,6-O-benzylidene-3-benzylthio-3-deoxy- α -D-altropyranoside. The direction of opening of the anhydro ring agreed with observations recorded in the literature (7-9) and with the requirement that ring opening proceed preferentially via the more stable trans diaxial transition state according to Furst and Plattner's rule (20, 21). The position of the benzylthio group was verified by desulphurization of the benzylthio ethers with Raney nickel (9, 22) to produce the corresponding deoxy monosaccharides. These were compared with authentic specimens prepared by the reduction with lithium aluminum hydride of methyl 2,3-anhydro-4,6-O-benzylidene- α -D-mannopyranoside and methyl 2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside (23).

When treated with sodium in liquid ammonia, methyl 4,6-O-benzylidene-2-benzylthio-2-deoxy- α -D-altropyranoside gave a good yield of solid methyl 2-deoxy-2-mercapto- α -D-altropyranoside which readily crystallized from alcohol. Reduction of methyl 4,6-O-benzylidene-3-benzylthio-3-deoxy- α -D-altropyranoside under the same conditions gave a colorless syrup which solidified on trituration with water. Attempts at purification by direct crystallization from a wide variety of solvents and solvent pairs were abortive. However, chromatography of the crude mercapto sugar on neutral alumina yielded bibenzyl in the initial fractions followed by a viscous colorless syrup which again readily solidified on trituration with water. Crystallization of this solid from ethyl propionate was slow, but large prismatic crystals were produced whose analysis agreed with the formulation of this substance as methyl 3-deoxy-3-mercapto- α -D-altropyranoside. It is thus seen that sodium in liquid ammonia removes not only the benzyl group from the sulphur atom but also provides a convenient route for the removal of the benzylidene group without affecting the glycosidic linkage. Simultaneous cleavage of the benzylidene group and desulphurization have been obtained by the use of a large excess of Raney nickel (8, 9). However, when no more than a fourfold excess of Raney nickel was employed, reductive desulphurization occurred unaccompanied by removal of the benzylidene group (9). Since 1,2;5,6-di-O-isopropylidene- α -D-glucofuranose (24) was quite unaffected by sodium in liquid ammonia, this reductive cleavage may be specific for the benzylidene group.

Hydrolysis of methyl 2-deoxy-2-mercapto- α -D-altropyranoside and the 3-mercapto isomer with *N* sulphuric acid gave yellow solids which charred on heating but would not melt. Infrared spectra showed the substances to be quite impure and afforded no information as to their structures. Neither they, nor the products obtained from attempts to prepare their acetyl, benzoyl, or 3,5-dinitrobenzoyl derivatives, could be obtained in crystalline form.

Freudenberg and Brauns (25) reported that treatment of 1,2;5,6-di-O-isopropylidene-3-O-tosyl- α -D-glucofuranose with hydrazine replaced the 3-tosyloxy group by the hydrazine moiety. The resulting compound has recently been shown unequivocally to have the allo configuration (26). Although Reichstein *et al.* (9, 27) have shown that both sodium methoxide and sodium methylmercaptide did not replace the tosyloxy group but merely caused detosylation, it was thought that the greater nucleophilic character of the benzylmercaptide might induce a reaction analogous to that obtained by Freudenberg and Brauns and thus lead to the formation of 3-deoxy-3-mercapto-D-allose. However, here again, reaction of sodium benzylmercaptide with 1,2;5,6-di-O-isopropylidene-3-O-tosyl- α -D-glucofuranose resulted only in detosylation with retention of configuration about C₃.

EXPERIMENTAL

All melting points are uncorrected.

Methyl 4,6-O-Benzylidene-2-benzylthio-2-deoxy- α -D-altropyranoside

Sodium (2 g) was dissolved in methanol (40 ml) containing benzyl mercaptan (2.6 g, 0.022 mole) (28). Methyl 2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside (5 g, 0.019 mole) (18, 19) was added and the mixture then refluxed under nitrogen for 2 hours. The solution, left standing overnight at room temperature, deposited crystalline material which was removed and recrystallized from ethanol. The methanolic mother liquor was diluted with water and extracted with chloroform. The chloroform extract was washed with water until neutral and dried with sodium sulphate. Elimination of the solvent gave a further quantity of crystalline material. Total yield of methyl 4,6-O-benzylidene-2-benzylthio-2-deoxy- α -D-altropyranoside was 7 g (95%). M.p., 136–137° C; $[\alpha]_D^{CHCl_3}$ at 22°, +90.6° ($c = 1.668$). Anal. Calc. for $C_{21}H_{24}O_6S$: C, 64.93; H, 6.23; S, 8.25. Found: C, 64.97; H, 6.22; S, 8.30.

Methyl 4,6-O-Benzylidene-3-benzylthio-3-deoxy- α -D-altropyranoside

Methyl 2,3-anhydro-4,6-O-benzylidene- α -D-mannopyranoside (19) was treated in a manner similar to that given the allo isomer with the exception that the reaction time was extended to 15 hours. Crystallization did not occur when the solution stood at room temperature overnight; therefore the reaction mixture was diluted with water and extracted with chloroform. The chloroform solution was washed until neutral and then dried with sodium sulphate. Removal of the solvent left a viscous syrup which solidified after trituration with ether. Recrystallization from methanol afforded colorless crystals. M.p., 105–106° C; yield, 88%; $[\alpha]_D^{CHCl_3}$ at 22°, +54.9° ($c = 1.436$). Anal. Calc. for $C_{21}H_{24}O_6S$: C, 64.93; H, 6.23; S, 8.25. Found: C, 64.90; H, 6.44; S, 8.18.

Methyl 2-Deoxy-2-mercapto- α -D-altropyranoside

Finely powdered methyl 4,6-O-benzylidene-2-benzylthio-2-deoxy- α -D-altropyranoside (5 g) was added to liquid ammonia (150 ml) in an Erlenmeyer flask cooled in dry ice. Small pieces of sodium metal were added to the solution, constantly stirred by a magnetic stirrer, until the blue color persisted for 10 minutes. At the end of this time, ammonium chloride was added until the blue color was discharged, whereupon the ammonia was allowed to evaporate, under a blanket of nitrogen to prevent oxidation of the mercaptan. The residue was extracted with chloroform (N_2) which, upon evaporation, left a colorless solid possessing a sweetish odor. Yield of crude product, 90%; m.p., 140–145° C. Recrystallization from ethanol, in which the compound was found to be quite soluble, yielded small colorless needles, m.p., 145–146° C; $[\alpha]_D^{CHCl_3}$, +95.2° ($c = 0.9352$). Anal. Calc. for $C_7H_{14}O_5S$: C, 39.99; H, 6.71; S, 15.25. Found: C, 39.95; H, 6.71; S, 15.14.

Methyl 3-Deoxy-3-mercapto- α -D-altropyranoside

Finely powdered methyl 4,6-O-benzylidene-3-benzylthio-3-deoxy- α -D-altropyranoside was subjected to a sodium-in-liquid-ammonia reduction under the same conditions as outlined above for the 2-isomer. On removal of the solvent from the chloroform extract, a colorless viscous syrup remained which solidified on trituration with water. A solution of this material in a benzene-methanol mixture (5:1) was passed through a column of neutral alumina prepared in benzene. The initial fractions contained bibenzyl and were discarded. Subsequent fractions yielded a colorless viscous syrup which solidified when triturated with water.

Several recrystallizations from ethyl propionate gave pure methyl 3-deoxy-3-mercapto- α -D-altropyranoside as large prismatic crystals. M.p., 85–87° C; $[\alpha]_D^{H_2O}$, +68.6°

($c = 1.428$). Anal. Calc. for $C_7H_{14}O_5S$: C, 39.99; H, 6.71; S, 15.25. Found: C, 40.08; H, 6.80; S, 15.44.

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THE RADIOLYSIS OF CYCLOHEXANE

IV. BINARY MIXTURES IN THE VAPOR PHASE¹

J. M. RAMARADHYA² AND G. R. FREEMAN

ABSTRACT

The variation of the hydrogen yield with the composition of binary gaseous mixtures containing cyclohexane and benzene, cyclohexene, or propylene is qualitatively similar to that in the liquid phase.

The quantitative experimental data were tested against several possible reaction mechanisms and two mechanisms gave straight-line plots.

One mechanism involved scavenging of hydrogen atoms. The values of the kinetic parameters derived from this mechanism might not be unreasonable in the mixtures of cyclohexane with cyclohexene or propylene. The values for benzene, however, seem less likely.

The second mechanism involved the transfer of energy (excitation or ionization) from cyclohexane to the second substance. The values of the ratio of the rate constants, k_7/k_6 , of the reactions



is about 10^3 times greater in the gas than in the liquid phase. Consideration of possible detailed mechanisms of reactions [6] and [7] indicates that this difference is reasonable if $C_6H_{12}^{**}$ is a positive ion rather than an excited molecule.

INTRODUCTION

The study of binary systems has helped considerably in the investigation of the primary chemical processes involved in radiation chemistry. When a solute is dissolved in a solvent and the solution irradiated, the yields of the products are frequently quite different than they would have been if the substances had been irradiated separately. If the solvent product yields are lowered, the solute is said to "protect" the solvent. Thus the amount of hydrogen from cyclohexane radiolysis is considerably lowered by the presence of benzene.

Such a protective action of the solute might be caused either by trapping the free radicals produced from the primarily excited and ionized molecules or by trapping the energy from these molecules.

Our aim was to study the protection role played by benzene, cyclohexene, and propylene in the decomposition of cyclohexane during irradiation in the vapor phase.

EXPERIMENTAL

Cyclohexane and benzene were Eastman-Kodak spectrograde. Cyclohexene was obtained from Matheson, Coleman and Bell. Propylene was Phillips Research Grade material. All the materials were used as obtained.

The apparatus and techniques employed in this investigation were the same as those previously described (1). Binary mixtures of cyclohexane with benzene, cyclohexene, or propylene were irradiated at 108°C with Po^{210} α -particles. The concentration of these protectors ranged from 0.8 to 100 mole% in each case.

The mixtures of cyclohexane with benzene or cyclohexene were prepared as follows. Liquid solutions of various concentrations of protector in cyclohexane were made. Two milliliters of a given solution was thoroughly degassed and then volatilized into a liter bulb, heated electrically to 108°C .

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The mixtures of cyclohexane with propylene were prepared by volatilizing the appropriate amount of cyclohexane into the liter bulb and then injecting the required amount of propylene, such that the total pressure in the bulb was about the same as in the preceding mixtures (ca. 360 mm).

The liter bulb contained a calibrated Po^{210} -plated source (nominally 100 mc). The source was calibrated by Fricke dosimetry, using $G(\text{Fe}^{+++}) = 5.5$ (1). The irradiation time was 2 hours. Approximately 0.01% of the sample was decomposed. The pressure of the vapors in the bulb was such that all the energy was absorbed from the α -particles (1).

The products were analyzed by a Toepler pump - McLeod gauge combination and by gas chromatography.

The major product was hydrogen, with smaller amounts of ethylene, ethane, acetylene, propylene, propane, a C_4 hydrocarbon, cyclohexene, and dicyclohexyl. Under the conditions used, only the hydrogen could be measured accurately as a function of protector concentration. The precision of the measurements was 3% or better.

RESULTS

The results are presented in Fig. 1. In these plots, the observed values of $G(\text{H}_2)$, the number of molecules of hydrogen produced per 100 ev absorbed, are plotted against the "electron fraction" of the protector. The broken lines in the plots indicate the hydrogen

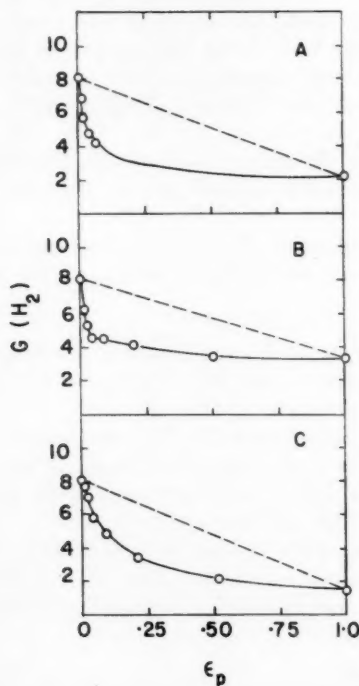


FIG. 1. Hydrogen yield as a function of protector concentration. ϵ_p = electron fraction of protector, P; (A) P = propylene; (B) P = cyclohexene; (C) P = benzene.

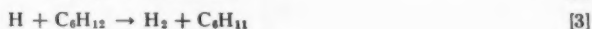
yield that might have been expected if there had been no interaction between the components and if the energy absorption were directly proportional to the electron fraction of the component (2, 3).

The variation of the hydrogen yield with the composition of the binary gaseous mixtures is qualitatively similar to that observed in the liquid phase (2, 3, 4). The hydrogen yield decreases quite rapidly with increasing protector concentration.

DISCUSSION

The experimental results were tested against several reaction mechanisms and two mechanisms were found to give straight-line plots. One mechanism involved scavenging of hydrogen atoms and the other involved energy transfer from cyclohexane to the protector. The two mechanisms will be treated separately.

I. Scavenging Mechanism



In the above equations, I represents the rate of formation of $\text{C}_6\text{H}_{12}^*$, which subsequently decomposes to produce a hydrogen atom; P represents the protector; and PH and P^- represent the corresponding radicals. Since the kinetic treatment is based on the hydrogen yield and since the formation of other products does not appreciably affect the hydrogen yield under the present conditions, the steps for the formation of other products have not been included. It may, however, be mentioned that a more complete mechanism involving some of the other products has been suggested by Freeman for the liquid-phase γ -radiolysis of cyclohexane-benzene (3) and cyclohexane-cyclohexene (4) systems.

By steady-state treatment of the above mechanism, it can be shown that

$$\frac{d(\text{H}_2)}{dt} = I \left\{ \frac{1 + k_5(\text{P})/k_3(\text{C}_6\text{H}_{12})}{1 + (k_4 + k_5)(\text{P})/k_3(\text{C}_6\text{H}_{12})} \right\}, \quad [i]$$

which may be rearranged to

$$\left\{ 1 + w \frac{(\text{P})}{(\text{C}_6\text{H}_{12})} \right\} \frac{I}{d(\text{H}_2)/dt} = 1 + v \frac{(\text{P})}{(\text{C}_6\text{H}_{12})} = \rho, \quad [ii]$$

where $w = k_5/k_3$, $v = (k_4 + k_5)/k_3$, and ρ represents the left-hand side of equation [ii].

The numerical values of $I/[d(\text{H}_2)/dt]$ can be determined from the experimental data (3). The experimental G values were corrected for the hydrogen produced by direct excitation of the protector (3).

By giving arbitrary values to w , sets of values of ρ can be calculated. A wide range of these sets of values were plotted against the ratio $(\text{P})/(\text{C}_6\text{H}_{12})$ to see if a straight line with an intercept of unity could be obtained for each of benzene, cyclohexene, and propylene. Such a line was obtained in each case (see Fig. 2). The values of the various ratios of rate constants derived from these plots are shown in Table I.

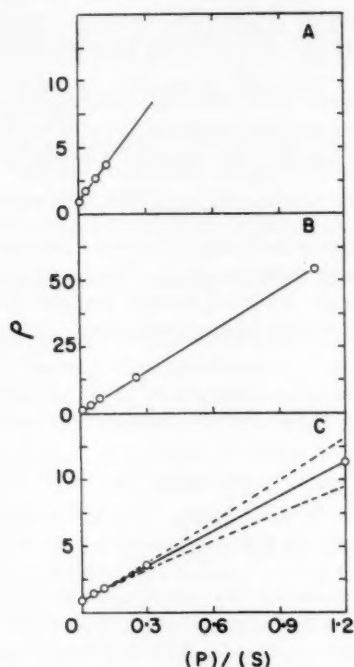


FIG. 2. Kinetic plots of mechanism I. $\rho = \{1 + w[(P)/(C_6H_{12})]\} I/[d(H_2)/dt]$; (A) P = propylene; (B) P = cyclohexene; (C) P = benzene (the upper and lower broken lines correspond to values of w of 3.0 and 2.0 respectively).

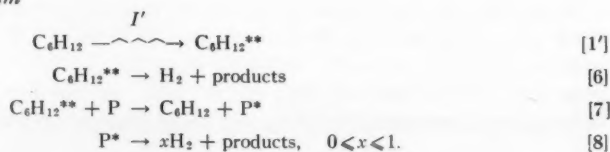
TABLE I
Values of rate-constant ratios obtained from mechanism I

P	k_6/k_3	k_4/k_3	k_4/k_5
C_6H_6	2.5 ± 0.2	5.9 ± 0.5	2.4
C_6H_{10}	25 ± 10	31 ± 19	1.2
C_3H_6	> 10	> 105	11

These values of the rate-constant ratios might not be unreasonable in the cases of cyclohexene and propylene. The value of k_6/k_3 obtained for benzene, however, is surprisingly high, even if the hydrogen atoms were epithermal. It implies that abstraction of hydrogen from benzene is 2.5 times faster than from cyclohexane. The smaller amount of hydrogen in benzene, and the stronger C—H bond in benzene than in cyclohexane, make this seem unlikely. It thus appears doubtful that the scavenging mechanism alone can account for the observed results.

Now let us consider the energy-transfer mechanism.

II. Energy-Transfer Mechanism



The x signifies that perhaps not every P^* results in the formation of an H_2 . Reactions [6] and [8] represent over-all processes and might comprise several steps each. Steady-state treatment of this mechanism yields

$$\{1+y(P)\}I'/[d(H_2)/dt] = 1+z(P) \quad [\text{iii}]$$

$$= \rho'$$

where $y = xk_7/k_6$, $z = k_7/k_6$, and ρ' represents the left-hand side of equation [iii]. Assuming arbitrary values for y , sets of values of ρ' were calculated and plotted against the protector concentration, (P), in an attempt to obtain a straight line with an intercept of unity (Fig. 3). The value of y that gave the desired line in each system, along with the slope of the line, z , and corresponding value of x , is presented in Table II.

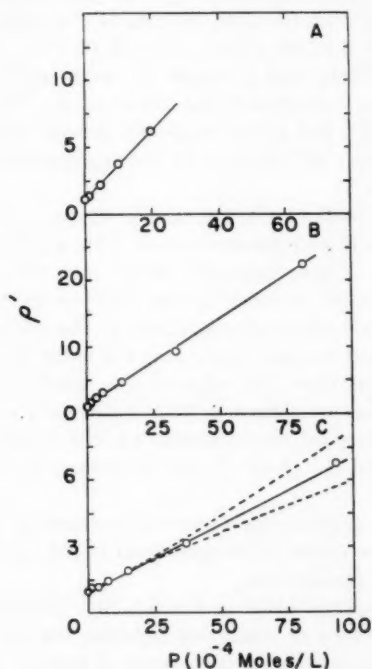


FIG. 3. Kinetic plots of mechanism II. $\rho' = \{1+y(P)\}I'/[d(H_2)/dt]$; (A) P = propylene; (B) P = cyclohexene; (C) P = benzene (the upper and lower broken lines correspond to values of y of 180 and 120 liter/mole respectively).

TABLE II
Values of kinetic parameters obtained from mechanism II

P	y (liter/mole)	x	z (k_7/k_6 , liter/mole)
C_6H_6	150 ± 18	0.25 ± 0.01	610 ± 25
C_6H_{10}	1200 ± 420	0.44 ± 0.01	2700 ± 800
C_3H_6	>1200	0.47 ± 0.01	>2570

The value of the ratio k_7/k_6 gives an indication of the ratio of the rate of energy transfer to the rate of decomposition of the excited cyclohexane species. The value of the ratio

k_7/k_6 in liquid cyclohexane + benzene was 0.78 liter/mole (3) and in liquid cyclohexane + cyclohexene, 0.54 liter/mole (4). Thus the value of this ratio in the gas phase is of the order of 10^3 greater than that in the liquid phase. This has three possible causes: (a) k_6 is much smaller in the gas than in the liquid phase; (b) k_7 is much larger in the gas than in the liquid phase; or (c) both.

Assuming that mechanism II is the correct one, the exact nature of $C_6H_{12}^{**}$ is not known. It is probably a positive ion or an electronically excited molecule.

Consider the possibility that $C_6H_{12}^{**}$ is a positive ion. If reaction [6] corresponds to the dissociative recombination of the ion and electron, k_6 would be several orders of magnitude smaller in the gas than in the liquid phase. It is believed that the lifetime of a positive ion in an irradiated liquid is of the order of 10^{-13} sec (5). However, under the present conditions of gas-phase irradiation (10^{13} ev absorbed/ml sec, k (ion-electron recombination) $\approx 10^{-6}$ ml/ion sec (6)), the lifetime of the positive ion is about 10^{-3} sec. Thus k_6 might be smaller by a factor of the order of 10^{-10} in the gas phase than in the liquid phase. It also seems likely that k_7 would be much smaller in the gas phase than in the liquid phase (reference 7 combined with reference 8). Thus it is possible that the value of the ratio k_7/k_6 in the gas phase would be several orders of magnitude larger than in the liquid phase (about 10^{10} divided by the appropriate ratio of k_7 values in the two phases).

If $C_6H_{12}^{**}$ were an electronically excited molecule, the rate of its decomposition might be the same in both the liquid and gaseous states. This would be especially true if the internal conversion of some of the electronic energy into vibrational energy occurs as rapidly as it is presently thought to occur (in the order of 10^{-13} sec (9)). Thus k_6 might be expected to be of the same order of magnitude in the gas and liquid phases. Most theories of electronic excitation transfer imply that the value of k_7 in the gas phase would be similar to or much smaller than the value in the liquid phase. The exciton theory (10) and the sensitized fluorescence theory (11) imply much smaller rate constants in the gas phase. If $C_6H_{12}^{**}$ were an electronically excited molecule, it appears that the value of the ratio k_7/k_6 in the gas phase should have been the same as or smaller than that in the liquid phase.

If the second mechanism applies, the observed increase in the value of k_7/k_6 by a factor of about 10^3 , when the phase is changed from liquid to gas, may be taken as an indication that $C_6H_{12}^{**}$ is a positive ion.

In the liquid-phase cyclohexane-benzene system, two 'protection' processes occur to comparable extents (3). The lack of resolution between the two gas-phase mechanisms in the present paper might be due to the occurrence of both. It is possible that the rate constants and concentrations are such that the two mechanisms cannot be resolved in the gas phase by the present technique. However, the apparent value of k_6/k_3 in the benzene-cyclohexane system is so high that the occurrence of only the scavenging mechanism is doubtful. Even if the energy-transfer mechanism contributed only a portion, say one half, of the over-all protection, the calculated values of k_7/k_6 would be of the same order of magnitude as those in Table II. The conclusion that the activated species taking part in the energy-transfer mechanism is probably a positive ion would still hold.

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THE LUMINESCENCE OF COMPLEX MOLECULES IN RELATION TO THE INTERNAL CONVERSION OF EXCITATION ENERGY

PART III. THE TOTAL EMISSION SPECTRA OF 1-NAPHTHOIC ACID¹

ROBIN M. HOCHSTRASSER

ABSTRACT

After excitation by 3130-Å light the anion of 1-naphthoic acid in ethanol solution internally converts to the triplet form of the acid. The excited-state equilibrium can be shifted by the addition of a base or an acid. Numerous total emission spectra of 1-naphthoic acid in various solvents can be understood in terms of some well-established principles governing non-radiative energy transfer processes within and between complex molecules.

No quantitative equilibrium studies are presented. The results indicate that the lowest excited states of the acid, singlet and triplet, are of π, π^* character. The lowest excited singlet state of the anionic form is most probably n, π^* , while the lowest triplet level is π, π^* .

INTRODUCTION

Parts I and II of this series were concerned with the influence of the excitation energy on the luminescence of complex molecules (1, 2). In this part the technique of total emission spectroscopy, i.e. the simultaneous measurement of fluorescence and phosphorescence and the relative yields of these processes, is applied to 1-naphthoic acid. In a previous paper (3) the emission spectra of 1,1'-binaphthyl were examined in various media as a function of temperature. If the electronic levels of 1-naphthoic acid are considered to be weakly perturbed versions of the levels of naphthalene, then the acid dimer structure is analogous to 1,1'-binaphthyl with the naphthalene rings about three times farther apart. The total emission spectra of the acid resemble, in their spectral location, the spectra of both naphthalene and the binaphthyls but the phosphorescence and fluorescence efficiencies are found to be quite different and strongly solvent dependent. Changes of this type must be related to variations of the non-radiative processes which occur after light absorption in the complex molecule.

The fluorescence and absorption spectra of 1-naphthoic acid and the 1-naphthoate ion have been used by Weller (4) to measure the pK of the acid and of the protonated acid. El-Bayoumi and Kasha (5) have measured solvent spectral shifts for the monomer and dimer acid. Preliminary observations of the emission spectrum of the dimer and monomer indicated that the exciton model of Kasha and McRae (6) could not explain satisfactorily the spectra of 1-naphthoic acid in various solvent systems. Both the ground state and excited molecules can undergo solvolysis reactions, the products of which have considerably modified electronic structures.

This part is a study of the photochemical processes which occur during the electronic excitation lifetime of an organic acid, and provides an interesting example of how the established principles of molecular spectroscopy may be employed to deduce the detailed mechanism of a photochemical reaction.

EXPERIMENTAL

The experimental details have been published previously (3). A monochromatic source was used to excite the luminescence. All the spectra were recorded spectrophotometrically on a modified Hilger E2 spectrograph. The solvents had optical densities of less than

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0.01/cm, and no emission was detectable from the pure solvents, on excitation with 3130-Å light. The coolant was ice-free liquid nitrogen. The spectra are not corrected for the response of the 1P28(RCA) photomultiplier. In order to estimate absolute phosphorescence-fluorescence yield ratios from the figures, the phosphorescence curves should be magnified by about 1.5 times.

Table I shows the estimated probable 0-0 transition energies for 1-naphthoic acid and

TABLE I

Solvent	Temp., °K	Origin of emission, $\text{cm}^{-1} \pm 40$		ϕ_F/ϕ_P^*
		Fluorescence	Phosphorescence	
Methylcyclohexane	300	28,330	—	—
Methylcyclohexane	77	29,680	19,880	0.10
Ethanol	300	26,950	—	—
Ethanol	77	30,340	19,830	1.36
Ethanol - KOH (0.05 M)	77	—	20,540	20

* ϕ_P/ϕ_F is the intersystem crossing ratio, being the ratio of the fluorescence and phosphorescence quantum yields. The values in the table were obtained by comparing the areas of the corrected emission spectra.

its conjugate base in various media. The phosphorescence to fluorescence yields in the last column of Table I are corrected for photomultiplier response.

Luminescence of Alkaline Solutions

The pK_a of 1-naphthoic acid is 3.7 units at 290° K. The ΔH of ionization in protic solvents for acids of this strength is usually very small (~ 1000 cal); therefore, pK_a may increase by about 1 unit when the temperature is reduced to 77° K. The acid should therefore be 50% ionized in a rigid ethanol glass at a concentration of about 2×10^{-4} mole/liter. In 0.05 M KOH - ethyl alcohol the acid is completely ionized at 77° K.

The pK_s (K_s , acid dissociation constant of the lowest singlet excited level) is 2-4 units higher than pK at 300° K (7). At 77° K, pK_s should be at least 7.8; therefore the acid is completely ionized in 0.05 M KOH at this temperature.

Figure 1 therefore represents the total emission spectrum of the acid anion. The

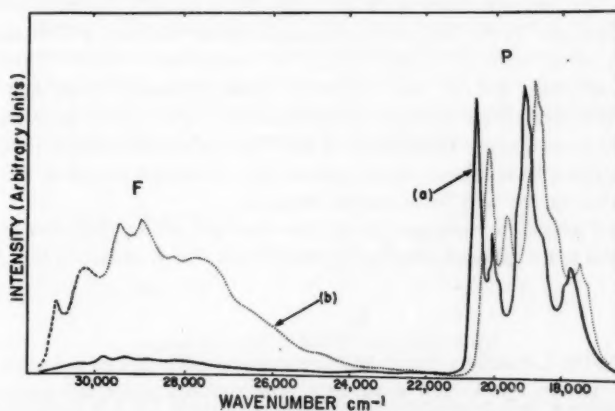


FIG. 1. Total emission spectrum of 1-naphthoic acid at 77° K. F and P indicate the fluorescence and phosphorescence regions.

(a) 1.1×10^{-5} mole/liter; solvent, ethanolic KOH (0.05 M).

(b) 2.0×10^{-4} mole/liter; solvent, ethanol.

outstanding feature of this spectrum is the extremely high ratio of phosphorescence to fluorescence yield. This is typical of the class of molecules whose lowest excited singlet levels are reached by $n \rightarrow \pi^*$ promotional transitions. For molecules with singlet ground states, fluorescence from $^1(n, \pi^*)$ levels is always weak because of the forbidden character of the transition. Non-radiative intercombinations with upper triplet levels of the molecule can proceed at the usual rate for polyatomic molecules (10^7 sec^{-1}) so that the phosphorescent level is populated in favor of fluorescence (8). The spectrum of 1-naphthoic acid in ethanol is shown in Fig. 1 for comparison.

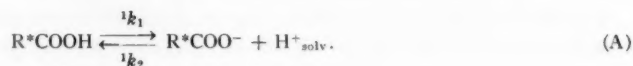
In view of the large gap between the origins of fluorescence and phosphorescence ($10,000 \text{ cm}^{-1}$), it is probable that the lowest triplet level of the anion is of $^3(\pi, \pi^*)$ character. Such a gap would be much larger than any previously measured splitting between an n, π^* singlet and triplet state. Further, qualitative estimates have proved that the half-life of phosphorescence for the acid and the anion are about equal. Thus there is good indication that states of the same nature are involved.

Luminescence of Ethanolic Solutions

As mentioned previously there are two absorbing species in solutions of the acid at low concentrations in ethanol. Absorption by the anion and the acid will give rise to two different emissions so the systems will be treated independently.

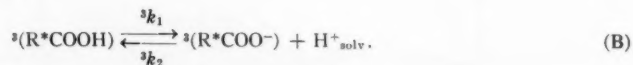
Primary Light Absorption by the Anion

The excited singlet (n, π^*) anion can undergo two reactions in solution at 77° K . Firstly, intersystem crossing to the triplet anion may occur; the half-life for this process is about 10^{-7} sec . The newly formed triplet is rapidly thermally equilibrated and the reverse reaction has a vanishing probability at 77° K . The singlet anion is also involved in the solvolysis reaction



The equilibrium constant for this dissociation is at most 1.3×10^{-8} (see previous section) and the hydrogen ion concentration is $2 \times 10^{-4} \text{ mole/liter}$ at 50% ionization in the ground state. The rate constant k_2 for the proton recombination reaction is diffusion controlled and should be within an order of magnitude of $10^{10} \text{ liters mole}^{-1} \text{ sec}^{-1}$. Thus the half-life of recombination is about $5 \times 10^{-7} \text{ sec}$. Once reformed, the acid could not ionize again within times comparable to its half-life of fluorescence. The anion may therefore form the excited acid by proton recombination *or* it may form the triplet anion; for the example chosen, these processes have about equal probability although at lower acid concentrations the latter alternative will be strongly favored.

The triplet anion may now undergo one of two courses: either radiative intercombination with the ground state (phosphorescence), with a half-life of close to 1 sec, *or* the proton recombination



The phosphorescence 0-0 transition of the ion is shifted by 1.8 kcal/mole to higher energy than the corresponding transition of the acid at 77° K . The value of $\text{p}K_T$ (acid dissociation of the triplet) at 77° K is therefore 5.1 units.

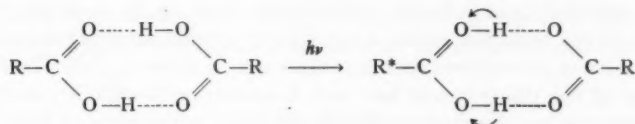
As for 1k_2 , the value of 1k_2 is about 10^{10} liters mole $^{-1}$ sec $^{-1}$ and therefore the half-life of recombination is 5×10^{-7} sec; 3k_1 is therefore 8.7×10^4 sec $^{-1}$. The half-life of emission for each of the triplet molecules in (B) is 1 sec, which means that less than 1.0% of the phosphorescence observed in ethanol solution is from the triplet anion. Figure 1(b) shows the total emission spectra from ethanolic solutions of 1-naphthoic acid. The fluorescence is from the acid singlet level and the phosphorescence is from the acid triplet level, both attained after primary light absorption by the anion, as described above. Some of the fluorescence may have originated from directly excited acid but under the present experimental conditions these could not be separated.

The phosphorescence-fluorescence yield ratio in ethanolic solution is high and could be altered by adding acid (e.g. H_2SO_4) in accordance with the above scheme.

The Luminescence of 1-Naphthoic Acid in Methylcyclohexane

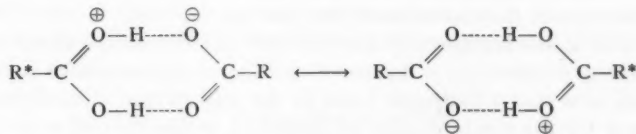
In this solvent the acid is dimerized completely at 10^{-3} mole/liter at 300° K (9). The heat of dimerization of carboxylic acids is usually around 10 kcal/mole so at concentrations as low as 10^{-6} mole/liter the acid will be completely dimeric at 77° K. It was not possible to glassify solutions more concentrated than 10^{-6} M without forming microcrystals which themselves have an intense emission in the blue region of the spectrum.

Weller has shown that the carbonyl oxygen becomes more basic in the lowest excited singlet state of the acid (10). The acidic oxygen also becomes more basic in this excited state, i.e., the acid is weaker. The protons in the hydrogen bridges of the dimer must therefore both be attracted towards the half of the dimer in which the excitation energy is localized.



It is unlikely that the protonated acid (excited) and the anion (unexcited) will separate completely as the former is still a very strong acid and the latter a very strong base.

Strictly, the excitation energy is not initially localized in one of the naphthalene rings. The electronic states of the separated conjugated systems are weakly coupled in the dimer and the excitation energy may be transferred non-radiatively between the two configurations. The half-life of transfer may be about 10^{-11} sec for weak coupling situations of this type. In the excited state the dimer is therefore stabilized by a resonance force interaction which may be represented as follows.



The total emission in Fig. 2(b) is interpreted as dimer emission. Owing to the very weak coupling between the rings, the emission spectra in Fig. 2 should not differ appreciably from the pure monomer emission. The phosphorescence to fluorescence yield ratio is very low for the dimer (1:10) and is similar to the value for unsubstituted naphthalene.

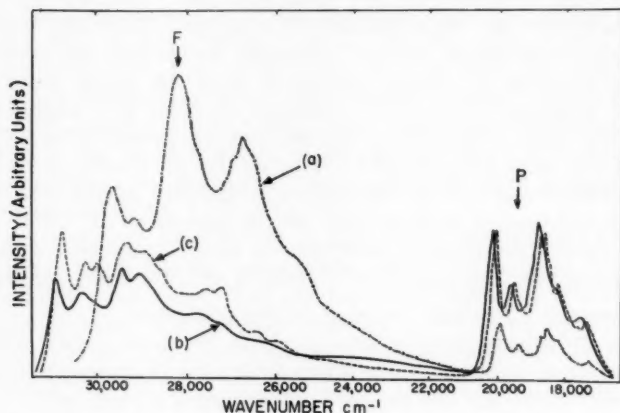


FIG. 2. Total emission spectrum of 1-naphthoic acid at 77° K. F and P indicate the fluorescence and phosphorescence regions.

- (a) 4.6×10^{-6} mole/liter; solvent, methylcyclohexane.
- (b) 4.6×10^{-6} mole/liter; solvent, methylcyclohexane - ether (0.25 M).
- (c) 4.6×10^{-6} mole/liter; solvent, methylcyclohexane - ethanol (0.026 M).

Low values for the phosphorescence yield are characteristic of molecules with lowest excited singlet states of π, π^* character. The transition moment for the singlet-singlet emission of 1-naphthoic acid is known to lie in the plane of the molecule (11). Thus the fluorescence observed from the dimer is $^1(\pi, \pi^*) \rightarrow ^1(\text{ground state})$ emission.

An enhancement of phosphorescence was expected on dimerization. The lowest excited electronic state of the dimeric acid has zero combination probability with the ground state of the dimer—if the structure of the planar dimer is the same as that in the crystal (12). The low probability of fluorescence should cause increased probability of non-radiative processes such as intersystem crossing and hence an increase in the ratio of phosphorescence to fluorescence yields compared to the monomer (6). However, this would not arise if *either* the dimer were twisted *or* if the dimer splittings were of the order of kT . Both of these conditions are possibly upheld in the present case (11).

Emission in Mixed Solvents

(I) The addition of a small amount of ethanol (0.5 M) to the dimeric solution in methylcyclohexane caused a marked increase in phosphorescence yield. This is shown in Fig. 2(c). The ethanol presumably breaks up the dimer and the previously discussed sequence of reactions in the excited state may occur.

(II) Figure 2(b) shows the effect of diethyl ether (0.5 M) on the dimer emission spectrum. As in (I) the fluorescence is decreased and the phosphorescence is increased. This experiment indicates that a hydrogen bond to the acid oxygen of naphthoic acid is the sole requirement for the establishment of ionization in the ground state, and suggests that the electronic environment of the carboxylic oxygen does not seriously affect the acid-base reaction in the neighborhood of the acidic oxygen.

(III) Figure 3(b) shows the effect of adding a small quantity of acetic acid (0.04 M) to the dimeric methylcyclohexane solution. The spectrum is broadened but the phosphorescence to fluorescence yield ratio is hardly altered from the dimer value. The acetic acid

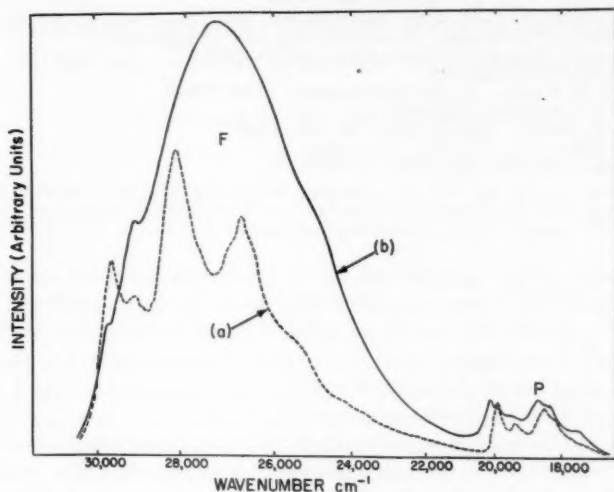
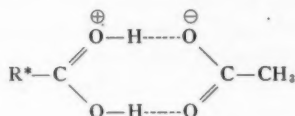


FIG. 3. Total emission spectrum of 1-naphthoic acid at 77° K. F and P indicate the fluorescence and phosphorescence regions.

- (a) 4.6×10^{-6} mole/liter; solvent, methylcyclohexane.
 (b) 4.6×10^{-6} mole/liter; solvent, methylcyclohexane - acetic acid (0.04 M).

is likely to be strongly hydrogen bonded to the naphthoic acid and the resulting species is a mixed dimer which is mainly undissociated in the ground state. In the excited state



the bridged protons would shift toward the basic and acidic sites of the naphthoic acid. It is unlikely that the mixed dimer would actually split into an excited protonated acid and an acetate ion, although the effect of excitation would be the reduction of the energy of dimerization. The influence of acetic acid on the emission spectrum is exactly what is expected on the basis of the explanations given in previous sections. Very similar results have been obtained for β -naphthoic acid. However, it was possible to obtain more concentrated solutions of the β -isomer in methylcyclohexane as no precipitation occurred in this case. The phosphorescence-fluorescence yield ratios were slightly lower than those for 1-naphthoic acid.

ACKNOWLEDGMENT

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INFRARED SPECTRA OF XANTHATE COMPOUNDS

III. ORGANIC SOLVENT EFFECT ON THE C=S FREQUENCY¹

L. H. LITTLE,² G. W. POLING, AND J. LEJA

ABSTRACT

The previously made absorption-band assignment (1) for the C=S stretching mode in xanthate-type compounds, 1020–1070 cm^{-1} , has been confirmed by the characteristic behavior of the C=S dipole in a range of different solvents (Bellamy and Rogasch (2)).

Assignments for the C=S stretching mode in xanthates, proposed by various investigators, cover the frequency range from 1000–1400 cm^{-1} and conflict with the assignments for the stretching vibrations of the C—O groups. It was felt necessary, therefore, to seek additional evidence to confirm our recent C=S band assignment (1) by solvent effects. Bellamy and Rogasch (2) found that a linear relationship exists between the frequency displacements ($\nu_{\text{vapor}} - \nu_{\text{solution}}$) of the C=S stretching vibrations in cyclic trithiocarbonates (dithioesters and some thioamides) and the frequency displacements of the C=O band in acetophenone, when studied in a particular sequence of solvents.

The same solvent sequence as that employed by Bellamy and Rogasch was used in the study of xanthate-type compounds. However, owing to the very low vapor pressures of solid xanthate compounds, their vapor-state spectra could not be obtained and the band displacements in the various solvents had to be represented relative to the frequency in cyclohexane. In the work of Bellamy and Rogasch cyclohexane solutions gave band frequencies close to those of the respective vapors. The behaviors of the two strong "xanthate bands", 1020–1070 cm^{-1} and 1200–1280 cm^{-1} , both of which had been assigned by various investigators (1, 3) to the C=S stretching mode, were contrasted; the shift of the 1020–1070 cm^{-1} band to lower frequencies (positive shift) in the solvent sequence from cyclohexane to tetrabromoethane confirms the fact that this band had been correctly assigned to the C=S stretching vibration.

EXPERIMENTAL

Materials.—Zinc *n*-butyl xanthate, *n*-butyl dixanthogen, and O-octadecyl, S-octadecyl dithiocarbonate were the same reagents which were previously used for the assignment of frequencies (1) and all analyzed 99%+ in purity. Solvents used were Eastman Kodak Company materials, designated "Specially pure for infrared spectroscopy", with the exception of dioxane, which was a C.P. grade reagent.

Procedure.—The spectra were recorded differentially (relative to pure solvent in the reference beam) on a Perkin-Elmer 221G spectrophotometer. The rotational lines of the ammonia-gas spectrum were used for frequency calibration (accuracy $\pm 1 \text{ cm}^{-1}$). Due to the intense absorption bands of many solvents in the spectral region of interest and due to the asymmetrical nature of the xanthate bands themselves, the accuracy of the frequencies determined in some solvents was probably of the order of $\pm 3 \text{ cm}^{-1}$.

RESULTS

Table I lists the frequencies and the relative displacements, $\Delta\nu = (\nu_{\text{cyclohexane}} - \nu_{\text{solvent}})$ cm^{-1} , of the two characteristic intense absorption bands, 1020–1070 and 1200–1280 cm^{-1} ,

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TABLE I
Absorption-band frequencies* and frequency shifts*

	1020-1070 cm ⁻¹ band						1200-1280 cm ⁻¹ band						Bellamy and Kogasch (2)							
	Zn <i>n</i> -butyl xanthate			<i>n</i> -Butyl dioxanthogen			O-Octadecyl, S-octadecyl xanthate			Zn <i>n</i> -butyl xanthate			<i>n</i> -Butyl dioxanthogen			O-Octadecyl, S-octadecyl xanthate			Ethylene trithiocarbonate	
	ν	$\Delta\nu$		ν	$\Delta\nu$		ν	$\Delta\nu$		ν	$\Delta\nu$		ν	$\Delta\nu$		ν	$\Delta\nu$		ν	$\Delta\nu$
Cyclohexane	1046	0		1028	0		1061	0		1238	0		1264	0		1214	0		1086	0
Diethyl ether	~1050	—		~1030	—		Insoluble			1203	35		1266	-2		~1218	-4		—	—
Carbon tetrachloride	1044	2		1027	1		1060	1		1244	-6		1266	-2		1218	-4		1083	3
Benzene	1062 1030	—		1023	5		1060	1		1241	-3		1268	-4		1221	-7		1078	8
Dioxane	Solvent absorption			1022	6		Insoluble			1208	30		1269	-5		Insoluble			—	—
Acetonitrile	1060 1037	—		1021	7		Insoluble			1235 1200 1180	—		1273	-9		Insoluble			1075	11
Nitromethane	Insoluble			1023	5		Insoluble			Insoluble			1274	-10		Insoluble			—	—
Methylene chloride	1039	7		1024	4		1057	4		1242	-4		1280 1248	—		1220	-6		1074	12
Chloroform	1040	6		1026	2		1058	3		1245	-7		1273	-9		Solvent absorption			1075	11
Bromoform	1038	8		1020	8		1054	7		1247	-9		1267	-3		1224	-10		1070	16
1,1,2,2-Tetrabromoethane	1037	9		1020	8		1056	5		1255 1213	—		1267	-3		Solvent absorption			1069	17
Solid or liquid	1045 _s	1		1022 _{liq}	6		1062 _s	-1		1209 _s	29		1264 _{liq}	0		1219 _s	5		—	—

*In cm⁻¹.

for the three compounds Zn *n*-butyl xanthate, *n*-butyl dioxanthogen, and O,S-di-octadecyl dithiocarbonate, in different organic solvents arranged in the same sequence as that used by Bellamy and Rogasch (2). For comparison, data given by Bellamy and Rogasch for ethylene trithiocarbonate are presented in the last column with the frequency displacements recalculated relative to the frequency in cyclohexane (instead of that of the vapor). Figure 1(A, B) shows selected spectra of two of the above-mentioned compounds in various solvents and in the 900–1300 cm^{-1} region.

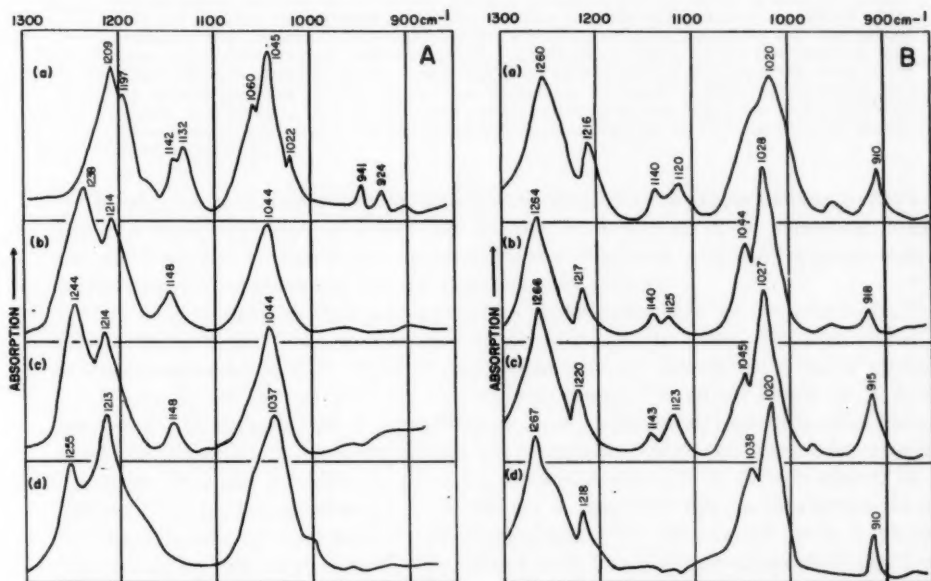


FIG. 1. Typical solvent spectra of Zn *n*-butyl xanthate and *n*-butyl dioxanthogen.
 A. Zn *n*-butyl xanthate in: (a) nujol mull, (b) cyclohexane, (c) carbon tetrachloride, (d) tetrabromoethane.
 B. *n*-butyl dioxanthogen in: (a) capillary film, (b) cyclohexane, (c) carbon tetrachloride, (d) tetrabromoethane.

DISCUSSION

The frequency shifts ($\Delta\nu$) of the 1020–1070 cm^{-1} bands, reported in Table I, are all positive and of the order of 0–9 cm^{-1} . The corresponding data of Bellamy and Rogasch, recalculated relative to cyclohexane, give a progressive change of $\Delta\nu$ from 0 to 7 cm^{-1} for dithioacetates and $\Delta\nu = 0$ –17 cm^{-1} for ethylene trithiocarbonate. The frequency displacements of *n*-butyl dioxanthogen and O,S-di-octadecyl dithiocarbonate exhibit more scatter (i.e. deviate more from linearity) than do those reported for dithioacetates and ethylene trithiocarbonates by Bellamy and Rogasch. However, since the general shifts of the 1200–1280 cm^{-1} band are toward higher frequencies (negative) in the same solvent sequence, the evidence clearly indicates that the 1020–1070 cm^{-1} band follows the typical C=S behavior while the 1200–1280 cm^{-1} band does not. This evidence confirms the assignment of the 1020–1070 cm^{-1} band to the C=S stretching mode in xanthate-type compounds and not the 1210–1230 cm^{-1} band as assigned by Felumb (3).

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THE ACIDITY OF NITROGUANIDINE AND ITS HOMOLOGUES¹

A. A. AMOS, P. D. COOPER, E. NISHIZAWA, AND GEORGE F WRIGHT

ABSTRACT

It has been shown that nitroguanidine, nitriminoimidazolidine, and 1-benzyl-2-nitriminoimidazolidine behave like urea by formation of potassium salts which completely hydrolyze in water. By contrast to true primary nitramines with which they might be considered to be tautomeric, the nitrimines are classed like urea as practically neutral compounds. Despite this ostensible tautomerism which was formerly evoked to explain the survival of nitroguanidine and nitriminoimidazolidine in alkaline solution it is now believed that the salts of nitroguanidine and nitriminoimidazolidine, from which the original nitrimines are regenerated upon acidification, are not intermediates, but rather end products, in the slow reaction with alkali. The intermediate is now postulated as an hydroxyisonitraminate anion from which the several products of the reaction are formed by appropriate fission. Presumably this anionic intermediate also is operative when tetraethylnitroguanidine or 1,3-dibenzyl-2-nitriminoimidazolidine is converted by alkali into tetraethylurea and 1,3-dibenzyl-2-imidazolidine respectively.

The chemistry of nitroguanidine and its homologues with alkalis seems to have been left in a state of confusion which may in part be due to an error appearing in one of our publications. In this paper we shall correct this error and shall suggest instead a more consistent explanation for the reaction with alkalis.

It is now recognized that nitroguanidine exists commonly as the nitrimine, $\text{H}_2\text{NC}(\text{NNO}_2)\text{NH}_2$, rather than as the tautomeric primary nitramine. Nitroguanidine does not react appreciably with alkali in aqueous solution in contrast to primary nitramines for which $K_a \approx 10^{-8}$ to 10^{-6} (1). Its electric moment is much lower ($\mu = 6.95$ D) than would be expected (2) if the substance were a nitramine, especially since the latter would be expected to have zwitterion characteristics. Also the ultraviolet absorption spectrum does not resemble those of known nitramines (2, 3) (which absorb at 225–240 $m\mu$) but its strong absorption at 265 $m\mu$ is near the 268 $m\mu$ absorption found to be characteristic of *sym*-tetraethylnitroguanidine (4) which certainly is a nitrimine. Essentially by the same criteria, the studies with 2-nitriminoimidazolidine (1), 1-nitro-2-nitriminoimidazolidine (5), and azobisnitroformamidine (6, 7) have shown that with few exceptions (8) most of the homologues of nitroguanidine have nitrimino-structures.

Nitrimines like these are formally analogous with urea and, indeed, there are similarities. Like urea, the acidity of nitrimines in water, as shown by potentiometric (2) and spectroscopic (9) examination, is negligible ($\text{p}K$ 12–14). The basicity of nitroguanidine has been reported as $\text{p}K_b = 14.5$ (10). Indeed the existence of salts such as the hydrochloride (11) in media minimal in content of water would indicate that the basicity is comparable with that of urea (K_b at 25°, 1.5×10^{-14}).

With bases, in nonaqueous media (potassium amide in liquid ammonia), urea will form a potassium salt. Under the same conditions potassium nitroguanidine (m.p. 155–156° C) is obtained in 49% yield. A salt of lesser purity (m.p. 149° C) is obtained in lower yield from molar potassium methoxide in methanol. These salts regenerate nitroguanidine when they are dissolved in water, but they can be crystallized satisfactorily from methanol containing potassium methoxide. The potassium nitroguanidine is recovered unchanged after a few hours in boiling dimethylformamide or acetonitrile, but alone it decomposes at 100° C (0.3 mm Hg pressure); cyanamide and dicyanamide have been found in the strongly basic residue.

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Contribution from the Department of Chemistry, University of Toronto, Toronto, Ontario.

The potassium nitroguanidine has been characterized, like its urea analogue, by reaction with benzyl chloride in absolute ethanol or in dimethylformamide. The yields of benzylnitroguanidine are 39% and 43% respectively, the remainder of the product being nitroguanidine. No trace of a benzylisonitramine, a characteristic product of primary nitramines, has been detected.

The acidimetric titration of benzylnitroguanidine in 50% aqueous ethanol (curve I, Fig. 1) shows that it is a nitrimine, since it does not react with 1 equivalent of alkali

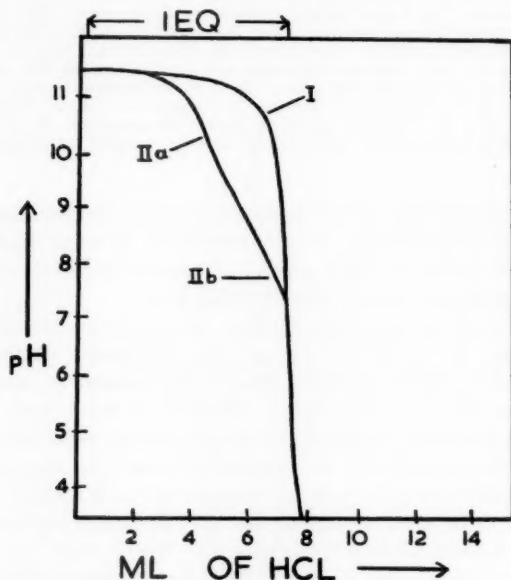


FIG. 1.

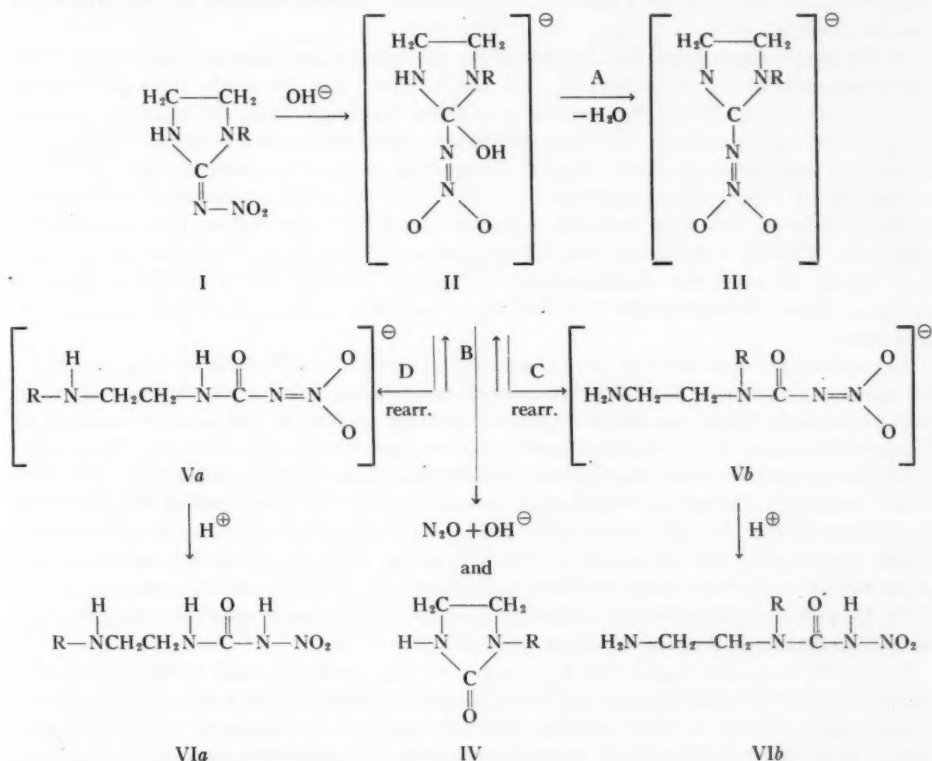
immediately after addition. However, when such a solution is aged for 62 hours its properties are altered according to titration curve II of Fig. 1. This curve shows two inflections: IIb is indicative of about 10% decomposition to an amine, while IIa shows that about 50% of the nitrimine has been converted to an acidic substance. Since 78% of benzylnitroguanidine is recoverable from the system, compared with 90% recovery from a freshly prepared solution, it is evident that the acidic substance must be present as the salt of isomeric benzylnitroguanidine.

In a former publication (1) from this laboratory, the isomer of non-salt-forming nitroguanidine (which isomer must have been present as the sodium salt in an aged alkaline solution) was designated as the nitramino form, $\text{NH}_2\text{C}(\text{NH})\text{NHNO}_2$. Likewise the sodium salt of nitraminoimidazoline had to be present, together with the sodium salt of 3- β -aminoethylnitrourea, after neutral nitriminoimidazolidine was aged in alkaline solution. From this experimental evidence it was postulated that nitraminoimidazoline was intermediate in the formation of 3- β -aminoethylnitrourea or its cyclic isomer, 2-hydroxy-2-nitraminoimidazoline.

This postulation is absurd. Nitraminoimidazoline cannot be an intermediate in the formation of 3- β -aminoethylnitrourea and, in the same system, be the source of recovered

starting material when the components of that system have neutralized an entire equivalent of alkali, since it has been shown that 3- β -aminoethylnitrourea in alkali does not yield any nitriminoimidazolidine when the latter system is acidified. Although the recovery of nitriminoimidazolidine by acidification of its aged alkaline solution definitely indicates that the salt of the nitramino tautomer is present, the latter cannot be an intermediate.

We suggest that the intermediate is the anion 2-hydroxy-2-imidazolidinylisonitraminate, II. The alkaline aging reaction may therefore be formulated as shown in the accompanying scheme (where R = H). After the isonitraminate ion, II, is formed



slowly from nitriminoimidazolidine, I, it may react by paths A, B, C, or D. Loss of water (path A) leads to the salt of the nitramine, III, from which I may be regenerated by acidification. Or the ion may decompose along path B, losing nitrous oxide and hydroxyl ion, to give the imidazolidone, IV (R = H). Finally the anion II (R = H) may rearrange by either path C or D to give the anions Va or Vb of 3- β -aminoethylnitrourea, VIa or VIb. When R = H, paths C and D are identical.

The same four paths will be involved in the alkaline reactions of nitroguanidines. Although all three products (urea, nitrourea, and nitroguanidine) have been detected from nitroguanidine, path A seems to be predominant. The large recovery of benzyl-nitroguanidine likewise indicates that path A is followed. On the other hand alkaline

treatment of nitriminoimidazolidine seems to follow chiefly path C, less along path A, and negligibly along path B.

It would seem then that the course of reaction is determined by the substituent groups. In conformity with this expectation we have now found that only paths B and D are followed when 1-benzyl-2-nitriminoimidazolidine (I, R = benzyl) is aged with alkali.

This substance may be prepared by treatment with benzyl chloride in hot ethanol of potassium nitriminoimidazolidine which is obtained in 47% yield by the method of Franklin and Stafford. The remainder of the reaction system is accounted as 2-nitriminoimidazolidine, and no trace of benzyl imidazolynlnitraminate or isonitraminate can be detected.

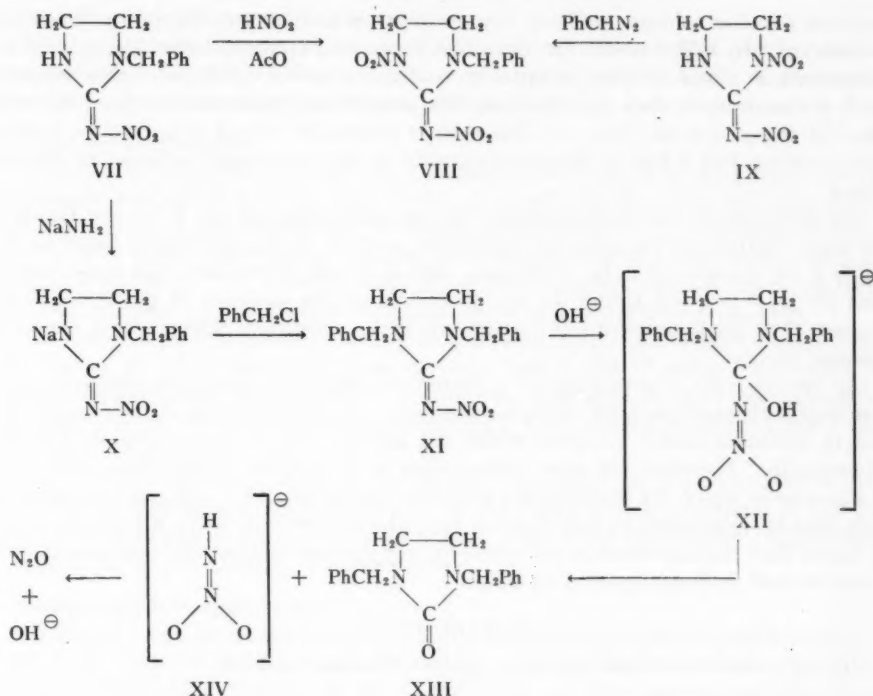
A 0.1 *N* solution of sodium hydroxide in water does not dissolve 1-benzyl-2-nitriminoimidazolidine (I, R = benzyl), but the solution may be made homogeneous by addition of ethanol. When the system is acidified within an hour, the starting material is recovered quantitatively. On the other hand, when the system is aged for 72 hours, a mixture is obtained in which none of the starting material is present. The mixture is comprised of 1-benzylimidazolidone (IV, R = benzyl) and a substance, the hydrochloride of which has been isolated, which we consider to be 3- β -benzylaminoethyl-1-nitrourea, VIa (R = benzyl). This latter assignment has been made because nitrous acid reacts to give the dinitrosamine $\text{PhN}(\text{NO})\text{CH}_2\text{CH}_2\text{N}(\text{NO})\text{CONHNO}_2$ but no nitrogen. Since the alternative VIb contains a primary amino group it is excluded by this test.

In previous publications (12, 13, 14) we have avoided a specific designation of structure for substances such as 3- β -benzylaminoethyl-1-nitrourea because of evidence showing that tautomeric forms (so-called ring-chain isomers typified in the present instance as 1-benzyl-2-hydroxy-2-nitriminoimidazolidine) are operative in this chemistry. Essentially the same reservation is implied in the formulations of equilibria between VIa, VIb, and II (R = benzyl); indeed this implication is supported by the instability of the substance designated as VIa. In 10% alkali this substance is slowly converted to 1-benzylimidazolidone, presumably via the anion II. The conversion of a nitriminoimidazolidine to an imidazolidone (IV) may thus lead to a somewhat complicated rate expression in which IV is formed both directly and indirectly from II. It is possible that difficulties of this sort have been encountered previously (15).

It may be true that I and VIb are present in quantities too small to be detected by our methods of isolation. Within the limits of these methods, paths A and C are excluded in favor of paths B and D, and this direction may be attributed to the substituent benzyl group in the intermediate anion II. However, it would be surprising if variations in ionic strength of the system did not divert the reaction into the other paths. Insufficient work has been done to make an assessment of this possibility.

The chemical reactions of 1-benzyl-2-nitriminoimidazolidine VII conform with those of analogous nitrimines. Thus it may be nitrated to 1-benzyl-2-nitrimino-3-nitroimidazolidine, VIII, which has also been prepared by treatment of 1-nitro-2-nitriminoimidazolidine (IX) with phenyldiazomethane. As has been shown above, benzyl-nitriminoimidazolidine (VII) does not itself form a stable alkali salt in aqueous solution. However, in nonaqueous media it reacts with sodamide to give a sodium salt, X, which, with benzyl chloride in ethanol, gives 1,3-dibenzyl-2-nitriminoimidazolidine, XI.

When this unquestionable nitrimine, XI, is treated with aqueous alkali the substance loses the elements of nitramide and becomes 1,3-dibenzyl-2-imidazolidone, XIII. It is



reasonable to postulate that the isonitraminate ion, XII, is intermediate in this conversion to the ketone and the anion, XIV, corresponding to nitramide. This ion, XIV, is known to decompose to nitrous oxide and hydroxyl ion. But this reaction series is only a special case of the alkaline aging reaction described over the formulation series I \rightarrow VI inclusive which is shown above. In this special instance substituent groups on nitrogen prevent reaction along paths A, C, and D, leaving only path C available. The same explanation applies to the alkaline conversion of *sym*-tetraethylnitroguanidine to *sym*-tetraethylurea (4).

Probably the two errors in our original publication on the acidity of nitroguanidines have by inadvertence led to criticism which has tended to obscure rather than clarify the chemistry of these substances. It is of interest that neither of these errors was actually detected by the critics.

The first error was quickly detected by us and it was reported shortly (6, 13) that, although neutral substances of appropriate constitution must be classified as nitrimines, it does not follow that the isomeric nitramino structure is applicable if the substance is moderately acidic. Such acidity may be induced by electron-withdrawing groups (such as the 1-nitro group in 1-nitro-2-nitriminoimidazolidine) without the occurrence of any atomic shift of a tautomeric nature.

Unfortunately the correction outlined above was not generally acknowledged (9). The evaluation of very weak acidities by spectroscopic means has obscured our definition of neutrality. In the sense that we used it, neutrality applies to the practical basis whereby a substance like nitroguanidine or nitriminoimidazolidine can be separated from an

aqueous alkaline solution without any evidence of sodium salt formation. Such compounds may be called neutral in the same sense that Hantzsch called the pseudo acid nitromethane a neutral form in order to contrast it to the *aci* form of this substance. Such a classification does not eliminate the pseudo acid nitromethane from its proper place in the pK_a scale. One can also write a resonance hybrid structure for ordinary nitromethane, but it has no direct relationship to the pseudo-*aci* behavior of this substance.

The situation is now unambiguous if in the publication by De Vries and Gantz (9) the term "nitramine" is read as "nitrimine" and all of the substances listed in their Table I are considered to be nitrimines. Also it should be realized that these valuable data by De Vries and Gantz do not contribute to the question of slow tautomerism because their analyses were not carried out under conditions which would reveal the isomeric process.

Our second error in stipulation of a tautomeric shift of nitrimine to nitramine as the first step in the reaction with alkali has now been corrected in terms of the initial formation of hydroxyaminate ion from which the sodium salt of the nitramine is formed subsequently. Therefore the slow tautomerism is an over-all experimental observation of a process in which the intermediate steps can lead to products additional to the nitrimine that is recoverable by acidification from the sodium salt of the nitramine. It is to be hoped that this clarification will eliminate the confusion about the reactions of nitroguanidine and its homologues with alkali.

EXPERIMENTAL

Melting points have been corrected against reliable standards.

Potassium Nitroguanidine

A solution was prepared of potassium metal (1.95 g, 0.05 g-atom) in 80 ml of anhydrous ammonia. Formation of potassium amide was allowed to proceed spontaneously. When the solution was colorless, 5.20 g (0.05 mole) of nitroguanidine was added, and the system was stirred while the substance dissolved. During the next 2 hours the white potassium salt precipitated. It was filtered off, m.p. 153.5–154°C, and then washed thrice with liquid ammonia, m.p. 155.5–156°C, 3.46 g (49.5%). Anal. Calc. for $CH_3KN_4O_2$: N, 39.4; K, 27.5. Found: N, 38.5; K, 27.1.

When the salt was heated for 1 hour at 65°C in 20 ml of anhydrous dimethylformamide and cooled, 75% (m.p. 145–146°C) was filtered off. The filtrate, after vacuum evaporation to half volume and dilution with diethyl ether, yielded 23% more, m.p. 133–137°C. Crystallization of the whole from 5 M methanolic potassium hydroxide gave a total yield of 98%, m.p. 152–153°C, not lowered by admixture with the original salt.

When the potassium salt was heated during 20 hours at 100°C (0.3 mm), gas was continually evolved. The residue in aqueous 10% nitric acid was filtered to remove nitroguanidine. Subsequent treatment of the filtrate with silver nitrate yielded yellow silver cyanamide.

Potassium 2-Nitriminoimidazolidine

This salt was prepared in 47% yield as described above. Admixture of the salt, m.p. 215–216°C, with 2-nitriminoimidazolidine gave a melting point depression. The salt was hydrolyzed by water to yield nitriminoimidazolidine. Anal. Calc. for $C_3H_5KN_4O_2$: K, 23.2. Found: K, 23.2.

Potassium 1-Benzyl-2-nitriminoimidazolidine

The reagent was not very soluble in liquid ammonia, but an 85% yield of salt was obtained, m.p. 226–227° C. Its hydrolyzate with water yielded 112% of the expected potassium content according to titration with acid.

1-Benzyl-2-nitroguanidine

To 0.57 g (0.004 mole) of potassium nitroguanidine in 20 ml of anhydrous dimethylformamide was added 0.75 ml (0.005 mole) of benzyl chloride. After 12 hours at 80° C this stirred system was filtered hot to remove sodium chloride. The vacuum-evaporated filtrate left a sticky solid which, extracted with diethyl ether and then water, left 0.365 g (43%), m.p. 170–172° C. Three crystallizations from absolute ethanol raised this melting point to 182–183° C, not lowered by admixture with authentic material (16).

A solution of 0.116 g (0.0006 mole) of this substance in 15 ml of hot absolute ethanol was cooled to 25° C, and 10 ml each of water and 0.1340 *N* sodium hydroxide were added. Back-titration with 0.1010 *N* hydrochloric acid showed exact equivalence with the alkali. When the system was evaporated to a 1-ml volume it yielded 0.104 g (90%) of benzylnitroguanidine, m.p. 178–179° C.

A similar solution was aged for 62 hours. Potentiometric titration with 0.1010 *N* hydrochloric acid showed, by the inflection on the curve, that $\frac{1}{2}$ equivalent of free alkali had been consumed in neutralization of a weak acid. From this system 78% of benzylnitroguanidine, m.p. 178° C, was recovered.

1-Benzyl-2-nitriminoimidazolidine

To 35 ml of dry benzene was added 5.2 g (0.04 mole) of 2-nitriminoimidazolidine and 2.0 g (0.051 mole) of sodium amide. The system was stirred for 8 hours at 70° C. The excess of amide was then destroyed carefully with absolute ethanol and then treated with 5.0 ml (0.044 mole) of benzyl chloride. After 8 hours of further stirring the system was cooled and the solvent was vacuum-evaporated. The residue was eluted with absolute ethanol and filtered to remove salts. The filtrate was decolorized with Darco and then evaporated to a 20-ml volume. The benzylnitriminoimidazolidine which precipitated was crystallized from ethanol, 3.6 g (41%), m.p. 148–149° C, not depressed by admixture with an authentic sample (17).

*1-Benzyl-2-nitrimino-3-nitroimidazolidine**(a) From Benzylnitriminoimidazolidine*

To a mixture of 7 ml (0.073 mole) of acetic anhydride, 7 ml of acetic acid, and 1 ml (0.024 mole) of 99% nitric acid stirred at 5° C was added slowly 0.5 g (0.0023 mole) of 1-benzyl-2-nitriminoimidazolidine. After an additional hour at 5° C the system was filtered to remove 0.5 g (88%), m.p. 150–152° C, decomp. After three crystallizations from 95% ethanol the melting point was raised to 154–154.5° C, decomp.

(b) From 1-Nitro-2-nitriminoimidazolidine

To a methanolic solution containing 0.003 mole of phenyldiazomethane (17) was added 0.5 g (0.0027 mole) of 1-nitro-2-nitriminoimidazolidine (III), and the system was warmed slightly to complete the evolution of nitrogen. Upon cooling to 4° C, 0.35 g of III precipitated. Upon evaporation to half volume, 0.15 g (72% of III consumed), m.p. 150–153° C, was obtained. Three crystallizations from ethanol raised this melting point to 154–155° C, not depressed by admixture with product from procedure (a). Anal. Calc. for $C_9H_{11}N_4O_4$: C, 45.2; H, 4.63. Found: C, 45.0; H, 4.41.

1,3-Dibenzyl-2-nitriminoimidazolidine

The treatment with benzyl chloride of the potassium salt from 8.8 g (0.04 mole) of 1-benzyl-2-nitriminoimidazolidine was carried out exactly in the manner of the benzylation of nitriminoimidazolidine. The product, 5.2 g (42%), m.p. 120–121° C, was thrice crystallized from chloroform (1.5 ml per g, +20° C to –75° C), m.p. 125–125.5° C. Some dibenzylimidazolidone, in one instance as much as 44%, was found in the crystallization mother liquors. Anal. Calc. for $C_{17}H_{18}N_4O_2$: C, 65.8; H, 5.81. Found: C, 65.5; H, 5.82. The five strongest spacings, in Angstroms, by X-ray diffraction using $Cu K\alpha$ radiation (Ni-filtered) are expressed as intensities: $[I/I_1]$ as [10] 2.79 [8] 5.04 [7] 4.11 [6] 2.10 [5] 2.29.

1,3-Dibenzyl-2-imidazolidone

To 0.176 g of 1,3-dibenzyl-2-nitriminoimidazolidine was added 7 ml of 20% aqueous sodium hydroxide. The solution was refluxed for 10 minutes, then chilled and extracted with 40 ml of diethyl ether. The extract, dried with magnesium sulphate, was evaporated, leaving 0.14 g, m.p. 85–90° C. Three crystallizations from absolute ethanol (4 ml per g) raised the melting point to 93–93.5° C, not depressed by admixture with the compound prepared by the method of Lob (19), yield 94%.

*1-Benzyl-2-nitriminoimidazolidine (I, R = Benzyl) with Alkali**(a) Recovery of I (R = Benzyl)*

To a cooled solution of 1.16 g (0.0053 mole) of 1-benzyl-2-nitriminoimidazolidine in 150 ml of absolute ethanol was added 187 ml of water containing 5.33 ml (0.012 mole) of 2.5 *N* aqueous sodium hydroxide solution. A 25-ml portion of this well-mixed system was extracted with three 20-ml portions of chloroform. The extract was dried by use of sodium sulphate and then was vacuum-evaporated to leave 0.089 g (100%) of I (R = benzyl), m.p. 146–148° C, authenticated by mixture melting point.

After several intervals of time, 25-ml portions were extracted and otherwise treated identically with that described above. The chloroform-extracted aqueous solution was acidified and again extracted with chloroform. The melting points of the evaporated extracts are recorded in the table below.

Reaction time (hr)	Recovered from alkaline solution		Recovered from acid solution	
	Wt. (g)	M.p. (°C)	Wt. (g)	M.p. (°C)
0	0.089	146–148	Omitted	
24	0.056	145–148	0.056	136–143
72	0.051	115–125	0.049	(gum)

(b) Isolation of 1-Benzyl-2-imidazolidone and 3-β-Benzylaminoethyl-1-nitrourea

A well-mixed system was prepared identical with that of procedure (a). The system was allowed to age for 62 hours at 25° C. After evaporation at 40° C (15 mm) to a volume of 30 ml the crystals were filtered off, twice washed with 2-ml portions of water, and dried at 40° C (15 mm), giving 0.432 g of 1-benzylimidazolidone, m.p. 126.5–128° C. The aqueous filtrate and washings were combined and extracted with 30 ml of chloroform. Evaporation of the extract left 1.60 g of the same substance, m.p. 126–128° C. The total yield, 64%, was identified by mixture melting point with an authentic sample (17).

The extracted aqueous filtrate was then acidified with 3 ml of 20% hydrochloric acid

and then was extracted with 20 ml of chloroform. The extract (containing 0.007 g of gum) was discarded while the aqueous phase was evaporated at 35° C (15 mm) to a 5-ml volume. The crystals were filtered off, 0.363 g (24%), m.p. 155–182° C. This 3- β -benzylaminoethyl-1-nitrourea hydrochloride was crystallized from methanol–methyl acetate and then from cold methanol–acetone mixture, m.p. 192–194° C (decomp.). The substance gave a strong Franchimont (20) and a positive Beilstein test. Anal. Calc. for $C_{10}H_{15}N_4O_3 \cdot HCl$: C, 43.7; H, 5.50; N, 20.5. Found: C, 43.9; H, 5.54; N, 20.5.

The pH of the filtrate from which this hydrochloride was removed was adjusted to 5.5 and some silica was filtered off. After 17 hours at 25° C stubby needles separated, which were filtered off and washed with 1 ml of ethanol to leave 0.075 g (6%), m.p. 170–171° C. This 3- β -benzylaminoethyl-1-nitrourea was recrystallized twice from hot water, m.p. 175–175.5° C. Anal. Calc. for $C_{10}H_{15}N_4O_3$: C, 50.4; H, 5.93; N, 23.6. Found: C, 50.7; H, 6.01; N, 23.1.

1-Benzylimidazolidone

A solution of 0.10 g (0.00036 mole) of 3- β -benzylaminoethyl-1-nitrourea hydrochloride in 10 ml (0.025 mole) of 10% aqueous sodium hydroxide solution was thrice extracted with 15-ml portions of diethyl ether. The ethereal extract contained about 10 mg of brown gum. After 2 days the aqueous phase deposited stubby needles which were filtered off and washed with 5 ml of water to leave 20 mg, m.p. 126–128° C, mixture melting point with authentic material not lowered.

When this 1-benzylimidazolidone was boiled 5 minutes with 2.5 *N* sodium hydroxide it was recovered unchanged. Also, when its solution in 6% hydrochloric acid was allowed to age at 25° C for 12 hours, and then evaporated at 40° C (15 mm) to a volume of 0.5 ml and neutralized with aqueous sodium bicarbonate, the substance was quantitatively recovered unchanged, m.p. and mixture m.p. 126–128° C.

3- β -*N*-Benzyl-*N*-nitrosaminoethyl-3-nitroso-1-nitrourea

To a solution of 0.274 g (0.001 mole) of 3- β -benzylaminoethyl-1-nitrourea (VIa, R = benzyl) in 8 ml (0.004 mole) of 1.8% aqueous hydrochloric acid at 0° C and under nitrogen was slowly added 0.276 g (0.004 mole) of sodium nitrite in 2 ml of water. This nitrite solution was added during 200 minutes from a mechanically driven hypodermic syringe. No gas was evolved and the solution remained clear and colorless until the last 30 minutes of the addition period.

When addition was complete a solid was filtered off and methanol-washed (0.083 g, 35%); it was unchanged starting material, m.p. 174–176° C, mixture m.p. not lowered. The filtrate was evaporated at 35° C (15 mm) to dryness and the residue was extracted with 5 ml of hot acetone. This extract was evaporated to a 2-ml volume and then was chilled to –80° C to precipitate 0.06 g (cold-acetone-washed), m.p. 172–175° C (decomp.). This 21% yield of dinitroso derivative was crystallized from absolute methanol, m.p. 184.5–185° C. The substance gave a strong Liebermann nitroso test (while the Liebermann test for the starting material was negative) and a positive Franchimont nitramine test. Anal. Calc. for $C_{10}H_{12}N_6O_5$: C, 40.6; H, 4.08. Found: C, 40.6; H, 4.05.

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METHYLATION OF SUGAR MERCAPTALS

II. L-ARABINOSE DIETHYL MERCAPTAL¹

G. G. S. DUTTON AND Y. TANAKA

ABSTRACT

Methylation of L-arabinose diethyl mercaptal in tetrahydrofuran with methyl iodide and silver oxide yielded mainly 2-O-methyl-L-arabinose and a trace of 5-O-methyl-L-arabinose. The identity of the major component was inferred by its behavior on electrophoresis and confirmed by the preparation of the crystalline amide. The polymethylated components were not examined. 2-O-Methyl-L-arabono- γ -lactone, previously known as a sirup, has now been obtained crystalline.

In Part I it was reported (1) that in the Purdie methylation of D-glucose diethyl mercaptal the 2-position was methylated exclusively but no methylation took place with other sugar mercaptals. This was attributed to the insolubility of the other mercaptals in methyl iodide. When the methylation was carried out in tetrahydrofuran not only D-glucose mercaptal but also other sugar mercaptals were found to be reactive towards Purdie's reagents; the qualitative investigation of these mercaptals has been described previously (1).

The present paper is the second in a series on the relative reactivities of hydroxyl groups in sugar mercaptals and describes the methylation of L-arabinose diethyl mercaptal in tetrahydrofuran. As with D-glucose diethyl mercaptal, the hydroxyl on C₂ of L-arabinose diethyl mercaptal is the most reactive to methylation in tetrahydrofuran. The primary C₆-hydroxyl group is also reactive but to a much lesser extent. No monomethylarabinoses were found other than the 2-O- and 5-O-methyl isomers, and a colorimetric estimation showed these to be present in the approximate ratio of 30:1.

L-Arabinose diethyl mercaptal was shaken at room temperature in tetrahydrofuran in the presence of silver oxide and drierite, in a quantity of methyl iodide adjusted so that a reasonable amount of monomethylarabinoses was obtained. Acid hydrolysis of the methylation mixture gave a mixture of methylated L-arabinoses which was shown by paper chromatography to contain, *inter alia*, two mono-O-methyl isomers. These two components were isolated by paper chromatography using butanone-water azeotrope as the developing solvent.

The fast-running component (R_f 0.30 in butanone-water azeotrope) was assumed first to be 5-O-methyl-L-arabinose (2), since it ran at the same rate as the latter on paper chromatography in butanone-water azeotrope. However, paper electrophoresis of this component showed that it was a mixture of 5-O-methyl-L-arabinose (M_r 0.80, faint) and a polymethylated arabinose (M_r 0.00, strong), the structure of which was not investigated. Since the amount of 5-O-methyl-L-arabinose produced in this methylation was very small, as shown by a faint spot on electrophoresis, it was not possible to isolate it and identify it by the preparation of a crystalline derivative.

The slow-running component (R_f 0.15 in butanone-water azeotrope) was shown to be electrophoretically homogeneous (M_r 0.33), and the crystalline amide was prepared (m.p. 131–132°C) from the sirup by oxidation with bromine followed by treatment with methanolic ammonia. Both 2- and 3-O-methyl-L-arabonamides have been reported

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Contribution from the Department of Chemistry, University of British Columbia, Vancouver 8, B.C. Presented at the 138th American Chemical Society meeting in New York, September, 1960.

(m.p. 131° C and 132° C, respectively (3)), but our amide was assumed to be the 2-*O*-methyl derivative from the fact that substitution of the 2-hydroxyl with a methyl group results in retardation of migration in electrophoresis (4). Admixture of our amide with an authentic sample prepared by the method of Jones, Kent, and Stacey (5) and of Hirst and Jones (6) showed no depression of the melting point.

Confirmation of the identity of the slow-moving component as 2-*O*-methyl-L-arabinose was obtained by showing that (a) the derived amide gave a negative Weerman test (7), (b) the infrared spectra of the amide of the unknown sugar and of the synthetic 2-*O*-methyl-L-arabonamide were superimposable, and (c) a mixed melting point of the unknown amide with an authentic sample of 3-*O*-methyl-L-arabonamide (m.p. 131–132° C) was 80–105° C. During the preparation of the authentic 2-*O*-methyl-L-arabonamide the 2-*O*-methyl-L-arabono- γ -lactone was obtained in crystalline form, m.p. 88° C.

In addition to these two monomethylarabinoses, a number of polymethylarabinoses and unreacted arabinose were also detected on paper chromatography, but they were not investigated further.

EXPERIMENTAL

Methylation of L-Arabinose Diethyl Mercaptal

L-Arabinose diethyl mercaptal (500 mg) was dissolved in 50 ml of dry tetrahydrofuran, and 500 mg of silver oxide and 3 g of drierite were added to the solution. Methyl iodide (10 ml) was added to the mixture which was then shaken at room temperature for 20 hours, during which time 30 ml of methyl iodide were added in aliquots of 10 ml at 5-hour intervals. The reaction mixture was filtered and evaporated *in vacuo* to a sirup which was then dissolved in 30 ml of chloroform, and a small amount of inorganic impurities was removed by filtration. The chloroform solution was evaporated *in vacuo*, and the sirup (564.3 mg) thus obtained was dissolved in a mixture of ethanol (10 ml) and concentrated hydrochloric acid (2.5 ml) and refluxed in boiling water for 5 hours. After neutralization with Duolite A-4 resin, the solution was evaporated *in vacuo* to give a light brown sirup (290.8 mg).

Chromatographic Separation of the Methylated L-Arabinoses

The sirup showed the following spots by paper chromatography: R_f 0.91 to 0.75 (two (?) components); 0.59, 0.47, 0.36, 0.30, 0.15, and 0.05 (butanone–water azeotrope); R_f 0.84 to 0.77 (two (?) components); 0.66, 0.57, 0.52, 0.45, 0.37, and 0.18 (ethyl acetate – formic acid – acetic acid – water, 18–1–3–4).

The sirup was chromatographed using butanone–water azeotrope for about 13 hours on Whatman No. 3MM paper previously washed with the same solvent. The components which corresponded to R_f 0.30 and R_f 0.15 (butanone–water azeotrope) were detected on both edges of the chromatogram, and the strips containing these components were extracted with boiling methanol. After three extractions the extract gave a very faint Molisch test. Yields of the fast- and slow-running compounds were 7.0 mg and 32.6 mg respectively. These two components were examined by electrophoresis (750–1000 v, 1.5 hours, 0.05 *M* sodium borate solution) and showed the following M_e values: slow-running component (R_f 0.15), M_e 0.33; fast-running component (R_f 0.30), M_e 0.80 (faint) and 0.00 (strong); synthetic 5-*O*-methyl-L-arabinose, M_e 0.80; (D-glucose, M_e 1.00).

A quantitative analysis of the fast-running component by the phenol – sulphuric acid

method (11) showed a ratio of 6:1 for the components with M_r 0.00 and 0.80. This gives approximately 30:1 for the ratio of 2-*O*-methyl-L-arabinose to the 5-*O*-methyl isomer.

Identification of the Slow-running Component as 2-O-Methyl-L-arabinose

The sirup (20.7 mg) was oxidized with bromine for 24 hours according to the ordinary procedure and the lactone (11.0 mg) was dissolved in 10 ml of ethanol (absolute), saturated with dry ammonia, and kept overnight at room temperature. Evaporation of the solvent gave 9.0 mg of sirup which was crystallized from ethanol - light petroleum ether. Yield: 45%, based on the monomethylarabinose. M.p. and mixed m.p. 131-132° C. Mixed m.p. with 3-*O*-methyl-L-arabonamide 80-105° C.

Synthesis of 2-O-Methyl-L-arabinose

This was prepared by the published method (6) from methyl β -L-arabopyranoside (m.p. 168° C, 4 g), anhydrous copper sulphate (50 g), and acetone (200 ml). The sirupy isopropylidene derivative (3.29 g) was methylated three times by Purdie's method and the product (2.45 g) hydrolyzed with *N* sulphuric acid for 4 hours on the steam bath. Neutralization (Duolite A-4 resin) and evaporation gave a sirup (1.67 g) which on chromatographic examination showed two strong spots (R_{arab} 3.76 and 10.7) and one weak spot (R_{arab} 1.0, butanone-water). Separation of the sirup on a cellulose-hydrocellulose column (9) using butanone-water yielded 691 mg of chromatographically pure 2-*O*-methyl-L-arabinose (R_{arab} 3.76, $[\alpha]_D^{22}$ 94.0° (*c*, 0.26 in water)).

When the preparation of this compound was attempted by refluxing for 24 hours a mixture of the sirupy glycosides (10 g) with anhydrous copper sulphate (50 g) and acetone (250 ml), the yield of chromatographically pure 2-*O*-methyl-L-arabinose was only 438 mg.

2-O-Methyl-L-arabono- γ -lactone

Synthetic 2-*O*-methyl-L-arabinose (173.2 mg) was oxidized with bromine, and the lactone (153.0 mg, 89.5%), obtained initially as a sirup, was crystallized from acetone or ethyl acetate as needles, m.p. 88° C; $[\alpha]_D^{20}$ -49.1° \rightarrow -46.3° (24 hours, *c*, 0.128 in water); λ_{max}^{nujol} 5.73 μ (8). Anal. Calc. for $C_6H_{10}O_5$: OMe, 19.2%. Found: OMe, 19.2, 19.5%. The lactone (111 mg) was converted to the amide (92 mg, 76%), which was recrystallized from ethyl acetate - acetone or ethyl acetate - methanol as fine needles; m.p. 131° C, lit. (6) m.p. 131° C. The infrared spectra of this amide and that obtained from the slow-running component were identical.

3-O-Methyl-L-arabinose

This was prepared by the courtesy of Mr. A. E. Barlay according to the method of Hirst, Jones, and Williams (10). The sugar had $[\alpha]_D^{22}$ 107° (*c*, 1.4 in water), and the derived 3-*O*-methyl-L-arabonamide, after recrystallization from ethyl acetate - petroleum ether, had m.p. 131-132° C.

ACKNOWLEDGMENTS

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THE ALKALOIDS OF CORYDALIS GOVANIANA¹

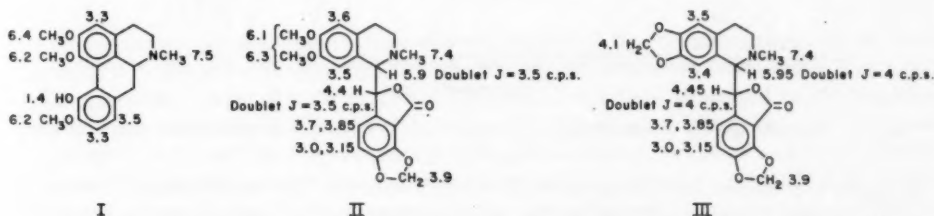
O. E. EDWARDS AND K. L. HANDA²

ABSTRACT

The Himalayan plant *Corydalis govaniana* (Wall. Tent.) has been shown to contain the alkaloids protopine, corlumine, bicuculline, and isocorydine, as well as fumaric acid and choline.

The alkaloids of the genus *Corydalis* have been the subject of intensive investigation (1). The species *govaniana* (Wall. Tent.), however, appears to have escaped chemical examination until the present work. It is native to the western Himalayas, where the inhabitants use the roots in treating skin diseases.

An alcohol extract of the dried ground root was concentrated to a syrup under reduced pressure, and the alkaloids extracted into dilute sulphuric acid. They were then separated using the general procedure devised by Manske (2) (see Flow Sheet I). Only known alkaloids were encountered: protopine, isocorydine (I), corlumine (II), and bicuculline (III) in the approximate ratio of 1:1:8:3. The latter two ran together with several solvent systems on paper, were not separated by chromatography on alumina, but could be partially separated by fractional crystallization. However, countercurrent distribution between benzene and buffer of pH 3 effected a clean separation of the two bases.



We were surprised to find the phthalide isoquinoline base corlumine (II) appearing, in part, among the phenolic bases. The lactone rings in it and bicuculline are hence readily opened by alkali, a fact supported by the fairly rapid shift of their ultraviolet absorption spectra in alkaline ethanol. The identity of the bases was surmised after study of their ultraviolet, infrared, and N.M.R. spectra and comparison of empirical formula and melting point with literature values. Finally, comparison was made with authentic samples kindly supplied by Dr. Léo Marion and Dr. R. H. F. Manske. The ultraviolet spectra and description of new salts of the alkaloids are documented in the experimental part. Our assignment of the main bands of the N.M.R. spectra have been indicated on the formula in τ (CDCl₃ solutions) (3). The infrared spectra of the alkaloids are reproduced in Fig. 1. Two features of the spectra of general interest are the N—CH₃ bands near 2800 cm⁻¹ and the OCH₃ bands near 2850 cm⁻¹. These supplement the sometimes

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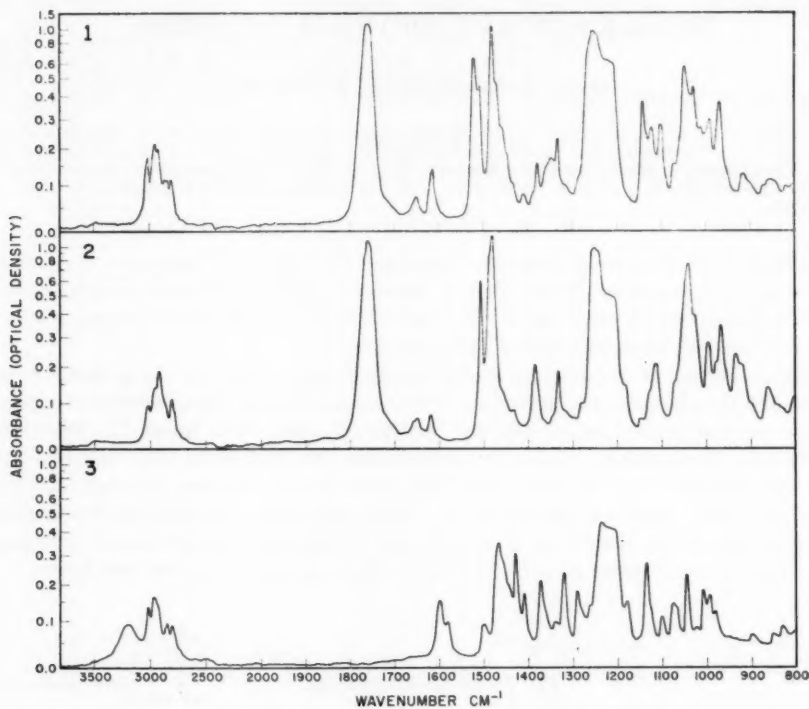


FIG. 1. Infrared spectra in chloroform in a 0.1-mm cell: 1, corlumine; 2, bicuculline; 3, isocorydine.

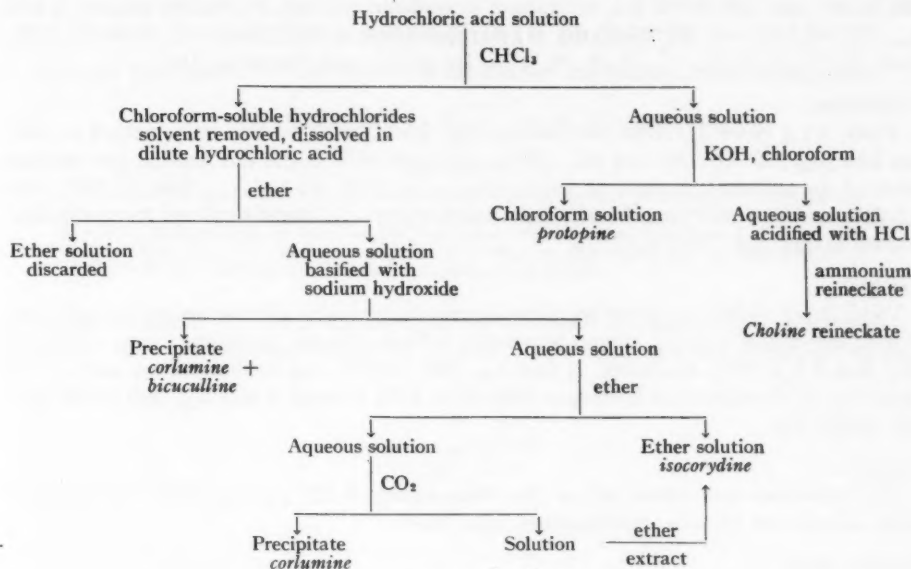
ambiguous evidence from analyses and N.M.R. spectra. The acidic material from the plant yielded fumaric acid, while the water-soluble part of the ethanol extract gave choline reineckate when treated with ammonium reineckate.

EXPERIMENTAL

Ultraviolet spectra were determined in 95% ethanol (intensities in ϵ are cited in parentheses), rotations in chloroform, and N.M.R. spectra in deuterochloroform with tetramethylsilane as internal standard. The pK_a' values were determined in the aqueous alcohol mixtures specified, by titration with *p*-toluenesulphonic acid in the same solvent. Melting points were determined on a Kofler hot stage.

Extraction and Separation

Roots of *Corydalis gowaniana* (Wall. Tent.) were collected in September 1960, air-dried, and ground. An exhaustive ethanol extraction of 5 kg of this material was made at room temperature. The extract was concentrated to a syrup under reduced pressure. The alkaloids were extracted from the syrup into dilute sulphuric acid. The acid solution was basified with ammonia and the alkaloids recovered by extraction into chloroform. After removal of the chloroform the residue was dissolved in 300 ml of 10% hydrochloric acid. After standing overnight, this solution was extracted six times with 200-ml portions of chloroform. The subsequent operations are shown on Flow Sheet I.



FLOW SHEET I

The corlumine-bicuculline mixture was not separated by chromatography on 20 times its weight of alumina, activity III. Five grams of the mixture was loaded in five Craig tubes (capacity, 10 ml of each phase) in benzene. It was then subjected to 100 transfers past phosphate-citrate buffer of pH 3. Tubes 15-45 contained one substance with peak concentration in tube 30. The contents of tubes 20 to 40 were combined and 3.6 g alkaloid recovered. After one recrystallization from methanol it melted at 160-161° and proved to be corlumine. Tubes 55-75 were mainly one alkaloid (peak concentration at tube 65) but a tailing out toward higher tube number suggested the presence of another. The contents of tubes 60 to 75 were combined. The alkaloid from these (1.3 g) melted at 197-198° after one recrystallization from methanol, and proved to be bicuculline. No pure alkaloids were obtained from the remaining tubes.

Corlumine

Yield, 17.2 g (0.36%). After four recrystallizations from methanol it melted at 162°; $[\alpha]_D^{25}$ 77° (c, 1.0); pK_a' (50% aqueous methanol) 6.3. Ultraviolet spectrum: λ_{max} 222 (30,640), 287 (3980), and 326 (5260) m μ , unchanged on addition of acid. In alkaline ethanol it had λ_{max} 219 (53,600) and 287 (7280) m μ . It did not depress the melting point of an authentic sample with m.p. 160°. The base formed a crystalline picrate, m.p. 204°. Found: C, 52.32; H, 3.71; N, 10.09. Calc. for $C_{27}H_{24}O_{13}N_4$: C, 52.92; H, 3.90; N, 9.14. Its perchlorate melted at 180-181° C. Found: C, 51.70; H, 4.70. Calc. for $C_{27}H_{21}O_8N_4 \cdot HClO_4$: C, 52.11; H, 4.56. Its picrolonate melted at 225°.

Bicuculline

Yield, 5.3 g (0.106%). After five recrystallizations from methanol this base melted at 199° and had $[\alpha]_D^{25}$ 131° (c, 1.6) and pK_a' (50% aqueous methanol) 6.2. It did not depress the melting point of an authentic sample of bicuculline, m.p. 198°. It had λ_{max} 225 (36,700),

296 (6390), and 324 (5870) $m\mu$, unchanged in acidified ethanol. In alkaline ethanol it had λ_{\max} 222 (48,440) and 293 (9540) $m\mu$. Its picrate melted at 202°. Found: C, 52.40; H, 3.31. Calc. for $C_{26}H_{20}N_4O_{13}$: C, 52.35; H, 3.35. Its picrolonate melted at 195°.

Isocorydine

Yield, 2.1 g (0.04%). After recrystallization from methanol this base melted at 186° and had $[\alpha]_D^{195}$ (c, 1.0) and pK_a' (80% methanol) 6.3. It did not depress the melting point of an authentic sample of isocorydine, m.p. 185°. It had λ_{\max} 220 (51,500), 266 (18,760), and 304 (6650) $m\mu$. In alkaline ethanol it had λ_{\max} 342 (19,440) $m\mu$. Its methiodide melted at 224° (lit. 224 (4)).

Protopine

Yield, 3.4 g (0.068%). After recrystallization from methanol this melted at 210° and showed no mixed melting point depression with authentic protopine, m.p. 211°. Its pK_a' was 8.2 in 90% methanol. It had λ_{\max} 290 (10,170) $m\mu$ unchanged on addition of alkali. In a 1 *N* solution of hydrogen chloride in 95% ethanol it had λ_{\max} 290 (9180) and 240 (9880) $m\mu$.

Choline

The reineckate was converted to the chloroaurate (0.215 g), m.p. 242°, undepressed when mixed with choline chloroaurate, m.p. 244°.

Fumaric Acid

The acid-insoluble part of the ethanol extract was extracted with hot water. On being cooled the solution deposited crystals of fumaric acid which sublimed above 200° and melted at 297° (sealed capillary); mixed m.p. with authentic fumaric acid, 297°.

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STERIODS AND RELATED PRODUCTS

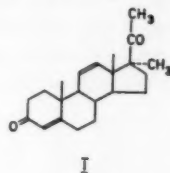
XVI. AN IMPROVED SYNTHESIS OF 11-DEHYDRO-17 α -METHYLPROGESTERONE^{1,2}

CH. R. ENGEL,³ G. JUST, AND R. BUTTERY

ABSTRACT

An improved synthesis of 11-dehydro-17 α -methylprogesterone, previously synthesized by this group, has been devised. The new hormone analogue has the same luteoid activity as 17 α -methylprogesterone; in this case, the 11,12-unsaturation has no potentiating effect on the progestational activity. Some stereochemical aspects of the Faworsky rearrangement of 17 α -halo-20-keto steroids are discussed in a preliminary fashion.

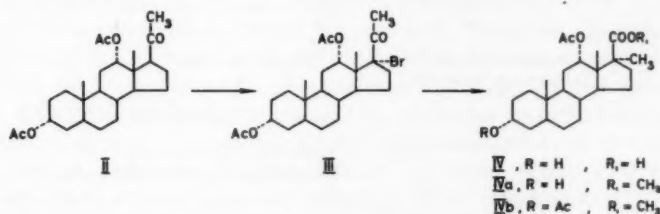
In a recent paper (2) this group reported the synthesis of a new progestational agent, 11-dehydro-17 α -methylprogesterone (I), in which were combined two chemical features



that independently increase the luteoid activity of the natural hormone, i.e. an 11,12-double bond and a 17 α -methyl group. While we had established that the new hormone analogue possessed marked activity, more material was needed for a quantitative biological evaluation.

Since the yields of two reaction sequences of the previously reported synthesis (2) had proved unsatisfactory, we devised an improved pathway for the preparation of the desired progestin.

One of these unsatisfactory sets of reactions had been the transformation of the starting material, 3 α ,12 α -diacetoxyprogane-20-one (II), to the 17 α -bromo derivative III and thence, by a Faworsky rearrangement, to ester derivatives of the 17 α -methyl etianic acid IV. Since it is known (compare ref. 3) that a Faworsky rearrangement of impure



17 α -bromo-20-ketones gives a poor yield of 17 α -methylated etianic acid derivatives, we considered that at least part of our difficulties stemmed from the fact that the amorphous

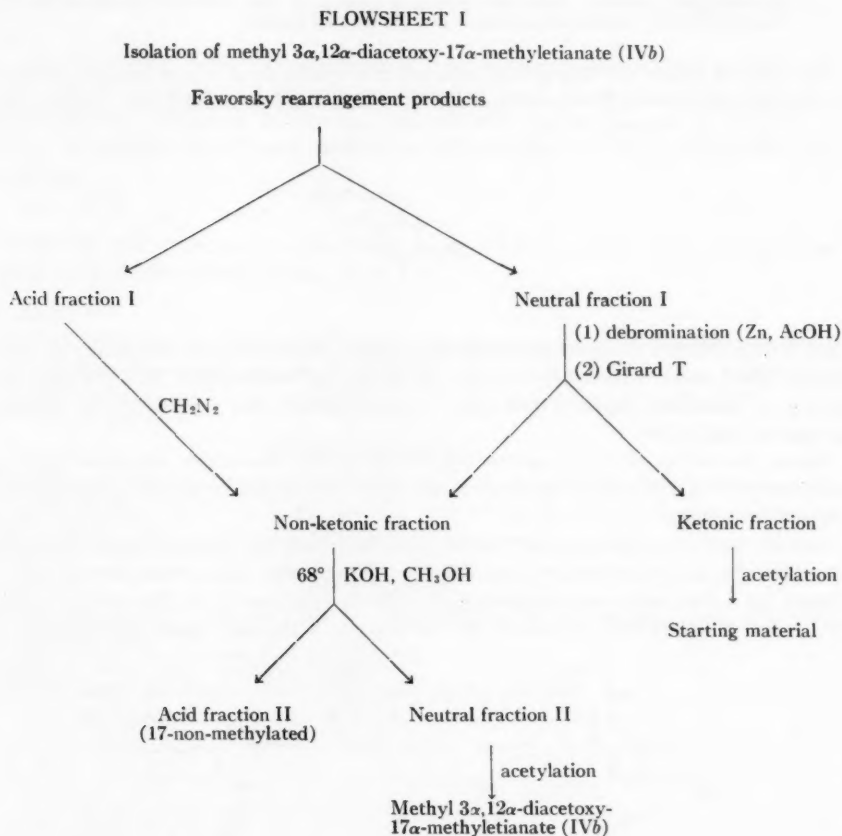
¹Manuscript received June 15, 1961.

Contribution from the Departments of Medical Research and Chemistry of the University of Western Ontario, London, Ontario, and the Department of Chemistry, Laval University, Quebec, Que. Some of the results reported in this paper were included in a communication presented at the 41st Annual Conference of the Chemical Institute of Canada, Toronto, Ontario, June, 1958.

²For paper XV of this series see reference 1.

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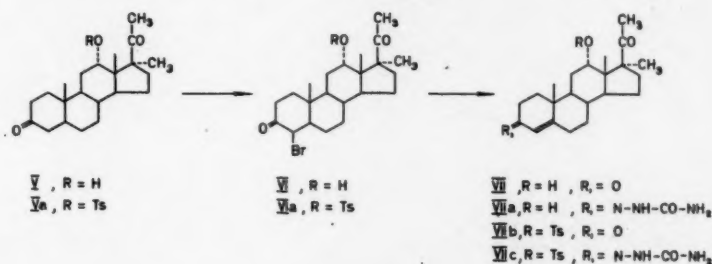
17 α -bromide III could not be isolated in the pure state. We were able to improve the yield of this reaction sequence by replacing the acid-catalyzed bromination of II with molecular bromine by a free-radical bromination with N-bromosuccinimide, using the procedure of Schock and Karpel (4). Furthermore, we simplified and improved the method of isolation of the desired rearrangement product by using a series of operations schematized in Flowsheet I and described in detail below under *Experimental*. Thus it was possible to raise the yield of the transformation of II to IVb by almost 50%, namely from 30–35% to 45–50%.



It is noteworthy that, as in the case of the previously reported Faworsky rearrangement of crude bromide III, we were not able to isolate any 17-epimeric rearrangement products, in spite of the fact that large amounts of material were used and carefully worked up. This is in accord with the results obtained when 17 α -bromopregnenolone acetate is treated with bicarbonate (3), and in contrast to those of the rearrangement with bicarbonate of 17 α -bromo-3 α -acetoxy-11,20-dione (5) (compare also the rearrangement of this compound with sodium ethylate, reported by Wendler *et al.* (6)). In the case of Faworsky rearrangements of 17 α -bromo-20-keto steroids without carbonyl functions

in ring C, by the action of bicarbonate, the mechanism proposed by Loftfield (7) seems unacceptable. Indeed, this mechanism consists in the concerted formation of a cyclopropanone intermediate which is opened by base; hence the reaction should proceed with inversion in 17 and result, in the case of a 17 α -bromo-20-ketone, in a 17 β -methyl-17-isoeticianic acid derivative. A synionic transfer of bromine from position 17 to 21, prior to the formation of the cyclopropanone intermediate, as postulated by Wendler *et al.* (6) (compare also an earlier proposal by Richard (8)), seems likewise improbable, at least in this instance, since the rearrangement of 21-halogenated 20-ketones gives a mixture of 17-epimeric etianic acid derivatives (compare ref. 9). A detailed discussion of this problem, together with new experimental data, will be reported in a forthcoming paper of this series.

A second unsatisfactory set of transformations in our previous synthesis of 11-dehydro-17 α -methylprogesterone was the penultimate sequence of reactions, consisting in the introduction of the Δ^4 -double bond into 12 α -tosyloxy-17 α -methylpregnane-3,20-dione (compare Va \rightarrow VIa \rightarrow VIIc \rightarrow VIIb (2)). The introduction of this double bond into the corresponding free 12 α -hydroxy derivative V (compare the transformations V \rightarrow VI \rightarrow VIIa \rightarrow VII) had also proved unsatisfactory. Since the analogous sequence of reactions



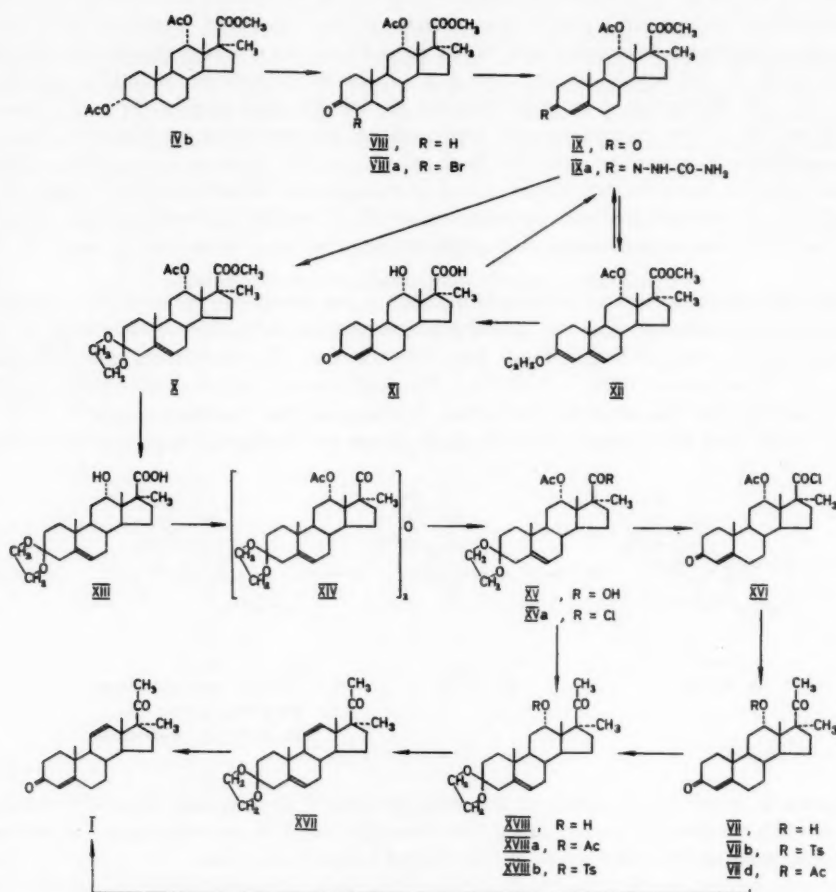
proceeded in much better yields in the case of methyl 12 α -tosyloxy-3-oxo-17 α -methyletiate (2), we decided to introduce the Δ^4 -double bond at an early stage of our new synthesis, prior to the elaboration of the methyl ketone side chain.

We transformed methyl 3 α ,12 α -diacetoxo-17 α -methyletiate (IVb) to methyl 12 α -acetoxo-3-oxo-17 α -methyletiate (VIII), as previously described (2). The 3-keto ester VIII was converted in high yield to the 4-bromide VIIIa by bromination with bromine in acetic acid, and the Δ^4 -double bond was introduced by McGuckin and Kendall's method (10), via the 4-unsaturated 3-semicarbazone IXa, in almost quantitative yield.

The Δ^4 -3-keto moiety of the resulting methyl Δ^4 -12 α -acetoxo-3-oxo-17 α -methyletiate (IX) was protected against the vigorous alkaline treatment necessary for the saponification of 17-methylated etianic esters, by formation of an ethylene ketal (X). Prolonged treatment of ester X with methanolic potassium hydroxide under pressure and at elevated temperature led, in 90% yield, to the 3-ethylenedioxy acid XIII.

Protection of the α,β -unsaturated ketone by the formation of an enol ether, which had proved satisfactory in previous experiments of this series (11, 12), gave somewhat disappointing results: the yield of the formation of enol ether XII was lower than anticipated and its conversion to the Δ^4 -3-keto etianic acid XI was not as simple as in the analogous cases which we described previously.

The 12 α -hydroxy-3-ethylenedioxy acid XIII was transformed to its acetate XV by



treatment with acetic anhydride in pyridine at reflux temperature and by hydrolysis with potassium carbonate of the 12 α -acetoxy anhydride **XIV** thus formed.

Whereas the carbonyl function of acid **XV** reacts readily with oxalyl chloride and whereas the acid chloride formed gives an excellent yield of a 17 α ,21-dimethyl-20-ketone upon treatment with dimethyl cadmium, the protecting ketal function in position 3 tends to be removed during this sequence of reactions, particularly in the course of the preparation of the acid chloride. Thus, the acetoxy ketal acid **XV** can be transformed in 87% yield to crystalline 12 α -acetoxy-17 α -methylprogesterone (**VII d**) without a separate hydrolysis step. If every trace of moisture is excluded during the preparation of the acid chloride, it is possible to obtain the 3-ethylenedioxy-20-ketone **XVIII a** as the main reaction product (approximately 70% yield of crude and 45% yield of purified product), from which the concomitantly formed Δ^4 -3,20-diketone **VII d** can be separated in the pure state in an approximate yield of 10% by crystallization and chromatography. This unsaturated diketone **VII d** can in turn be converted in over 50% yield to the monoketal

XVIIIa by the usual treatment with ethylene glycol and *p*-toluenesulphonic acid in boiling benzene. The retention of the ketal group in position 3 is desirable because alkaline hydrolysis of the 12 α -acetate requires, in the presence of a 17-methyl group, relatively drastic conditions (compare ref. 2) to which a free Δ^4 -3-ketone should not be exposed.⁴

The hydrolysis of acetate XVIIIa with methanolic potassium hydroxide proceeded in almost quantitative yield. Tosylation of the resulting hydroxy adduct XVIII was slow, but the desired 12 α -tosylate XVIIIb was obtained in 78% yield when care was taken to avoid hydrolysis of the ketal function during the working up. Dehydrotosylation was achieved in good yield by chromatography on activated aluminum oxide at elevated temperature, as described in the previous paper of this series (1) (compare also ref. 13), and the Δ^4 -3-keto moiety was set free by an exchange reaction with acetone in the presence of *p*-toluenesulphonic acid at room temperature (compare ref. 14). The resulting product was identical with authentic 11-dehydro-17 α -methylprogesterone (I), previously prepared by our group (2).

Doctors P. Perlman and M. Eisler of the Schering Corporation, Bloomfield, N.J., kindly tested the new hormone analogue I for progestational activity, in the Clauberg assay. They found that the product was, upon parenteral administration, two to three times as active as progesterone, hence of the same activity as 17 α -methylprogesterone (3). Evidently, the additional presence of the Δ^{11} -double bond, which raises the progestational activity of progesterone by a factor of 3 (15), had in this instance no potentiating effect. This is interesting because it is well established that in the majority of cases the inclusion in one molecule of more than one chemical feature which independently raises the same hormonal activity leads to potentiation of the biological effect. However, the finding is not entirely unexpected since Meystre and Wettstein (16) reported that 11-unsaturation of 17 α -ethinyltestosterone even lowered the progestational activity. It may be tempting to speculate that the enhancement of progestational activity brought about by an 11-double bond is confined to progesterone itself, or possibly to progestins with an unmodified methyl ketone side chain; that is to say, that this activity-enhancing effect of the 11-double bond could be due to an indirect effect on the interaction of the side chain with the receptor. However, more experimental data on 11-unsaturated progestins are needed before any valid conclusion can be reached concerning the mechanism by which this double bond exerts its effects on progestational activity, in the case of 11-dehydroprogesterone.

EXPERIMENTAL^{5, 6, 7}

17 α -Bromo-3 α ,12 α -diacetoxy pregnane-20-one (III)

To a hot solution of 49.872 g of 3 α ,12 α -diacetoxy pregnane-20-one (II) in 500 cc of dry carbon tetrachloride, 35.8 g of N-bromosuccinimide was added. The mixture was stirred, and irradiated for 9 minutes with a 660-watt photo flood lamp at reflux temperature. The product was cooled and filtered over sodium sulphate and the filtrate was washed

⁴It is possible to transform the Δ^4 -3-keto-hydroxy acid XI without protection of the alcohol function directly to Δ^4 -12 α -hydroxy-17 α -methylpregnene-3,20-dione (VII), which in turn can be converted to the tosylate VIIb and thence to 11-dehydro-17 α -methylprogesterone; however, as one would expect, the yield of this transformation is low.

⁵The melting points were taken in evacuated capillaries and the temperatures were corrected.

⁶The microanalytical work was performed by Mr. J. F. Alicino, Metuchen, N.J., and Drs. F. and O. Schwarzkopf, Woodside, N.Y.; we wish to express our sincere appreciation to them.

⁷For chromatography, Merck aluminum oxide was treated as described in footnote 18 of reference 13; cf. also footnote 18 of reference 11. We sincerely thank Merck and Company, Montreal, for the generous gift of aluminum oxide.

with cold 10% sodium bisulphite solution and with water. After having been dried over sodium sulphate, the solvent was removed *in vacuo*. The remaining crude amorphous bromide III (73 g) was used without further purification in the following reaction.

Methyl 3 α ,12 α -Diacetoxy-17 α -methyletiane (IVb)⁸

To a solution of the above-mentioned crude bromide III (73 g) in 2.47 l. of methanol, a solution of 138 g of potassium bicarbonate in 480 cc of water was added. The mixture was refluxed for 4 hours and its volume was reduced *in vacuo* to 600 cc. The product was poured into 6 l. of water and the precipitate was extracted with ether. The ethereal solution was washed with water, dried over sodium sulphate, and taken to dryness, thus affording 47.46 g of "neutral fraction I". The aqueous alkaline phase remaining after the extraction was acidified with sulphuric acid to a congo blue reaction and the resulting mixture was extracted with chloroform. The organic solution was washed with water, dried over sodium sulphate, and the solvent was removed. Thus 5 g of "acid fraction I" was isolated.

"Neutral fraction I" was dissolved in 750 cc of acetic acid and 75 cc of water. Then, at 60°, 75 g of zinc powder was added, portionwise and with repeated shaking, and the mixture was subsequently heated to 85° for 45 minutes with repeated shaking. The product was cooled and filtered and the filtrate was extracted with ether; the ethereal solution was washed repeatedly with dilute hydrochloric acid, with sodium carbonate and sodium bicarbonate solutions, and with water, and was then dried over sodium sulphate. Evaporation of the solvent afforded 46.06 g of a light yellow oil.

To a solution of this product in 460 cc of absolute ethanol and 46 cc of acetic acid, 51.5 g of freshly recrystallized Girard T reagent was added. The mixture was refluxed for 45 minutes, allowed to cool, and subsequently poured into 4.22 l. of an iced 0.15 *N* sodium hydroxide solution. The product was extracted with ether, the ethereal solution was washed with water and dried over sodium sulphate, and the solvent was removed. Thus there was obtained 28.16 g of the "non-ketonic fraction". The alkaline solution was acidified with sulphuric acid and the resulting product was extracted with ether. The ethereal solution was washed with iced sodium bicarbonate solution and with water and was dried over sodium sulphate. Evaporation of the solvent gave 23.87 g of the "ketonic fraction".

A solution of the "ketonic fraction" (23.87 g) in 82 cc of pyridine was refluxed for 90 minutes with 41 cc of acetic anhydride with the exclusion of moisture. The usual working up gave 24.1 g of an amorphous product. Chromatographic purification on aluminum oxide afforded 16.234 g of authentic starting material, 3 α ,12 α -diacetoxypregnane-20-one (II), m.p. 117–120°.

"Acid fraction I" (5.0 g) was dissolved in 80 cc of absolute methanol and 119 cc of absolute ether. To this solution was added, at 0°, 130 cc of a 2% ethereal diazomethane solution. The mixture was allowed to stand overnight at room temperature. The excess diazomethane was neutralized with acetic acid and the solvents were removed. The resulting methylated product (5.7 g) was combined with the "non-ketonic fraction". This mixture was refluxed for 4 hours in 570 cc of a 6.8% methanolic potassium hydroxide solution. After addition of 140 cc of water, the volume was reduced *in vacuo* to 200 cc and another 70 cc of water was added. The solution was now reduced *in vacuo* to 170 cc and then poured into 2.6 l. of distilled water. The mixture was extracted with ether and the ethereal solution was washed with water, treated with sodium sulphate, and taken to dryness. Thus 20.2 g of "neutral fraction II" was obtained. The aqueous alkaline residue

⁸Compare Flowsheet I.

of the ether extraction was acidified with sulphuric acid to a congo blue reaction and was extracted with chloroform. The organic solution was washed with water and dried over sodium sulphate. Evaporation of the solvent afforded 10.1 g of "acid fraction II", containing 17-non-methylated acids.

A solution of "neutral fraction II" (20.2 g) in 65 cc of pyridine was refluxed for 90 minutes with 33 cc of acetic anhydride with the exclusion of moisture. The usual working up gave 25.35 g of a partly crystalline product. Recrystallization from methanol gave 11.987 g of methyl 3 α ,12 α -diacetoxy-17 α -methyletiate (IVb), m.p. 159–161°. Chromatographic purification of the mother liquors on aluminum oxide gave another 5.126 g of IVb, m.p. 158–160°. The identity of this product was established by mixed melting point with an authentic sample and by comparison of the infrared spectra. In consideration of the recovery of starting material, the yield of methyl 3 α ,12 α -diacetoxy-17 α -methyletiate (IVb) from 3 α ,12 α -diacetoxy-pregnane-20-one (II) amounted to 47.5%. No 17 β -methyl-17-isoetianate could be obtained.

Methyl Δ^4 -12 α -Acetoxy-3-oxo-17 α -methyletiate (IX)

(a) Methyl 3 α ,12 α -diacetoxy-17 α -methyletiate (IVb) was transformed to methyl 12 α -acetoxy-3-oxo-17 α -methyletiate (VIII) as previously described (2). To a solution of 2 g of this keto ester VIII, m.p. 149–150°, in 40 cc of acetic acid were added a drop of hydrogen bromide solution in acetic acid and subsequently, dropwise and with stirring, over a period of 30 minutes, 5.9 cc of a 0.845 *M* bromine solution in acetic acid. The mixture was stirred for another 10 minutes and then poured into 500 cc of ice water. The precipitate was extracted with ether and the ethereal solution was washed with iced potassium bicarbonate solution and with water and was dried over sodium sulphate. Removal of the solvent *in vacuo* gave 2.56 g of crude crystalline methyl 4 β -bromo-12 α -acetoxy-3-oxo-17 α -methyletiate (VIIIa). Recrystallization from methanol-ether yielded 1.463 g of bromide VIIIa, melting between 177.5 and 179.5°, and 169 mg of slightly less pure bromide VIIIa, melting at 172–175°.

The mother liquors (900 mg) were debrominated in the usual fashion (see above) with 2 g of zinc dust in 22 cc of 90% acetic acid. Thus 636 mg of crude saturated 3-keto ester VIII, m.p. 115–125°, was recovered; recrystallization from ether-hexane gave 330 mg of pure ester VIII, m.p. 142.5–144.5°. In consideration of this recovery of pure starting material, the yield of bromide VIIIa amounted to 81.8%.

A solution of 1.369 g of bromide VIIIa, m.p. 177.5–179.5°, in 43 cc of absolute chloroform and 71 cc of *t*-butyl alcohol was flushed with carbon dioxide. Freshly recrystallized semicarbazide (434 mg) was added and the reaction mixture was again flushed with carbon dioxide and the flask was sealed. The mixture was occasionally shaken during 150 minutes. The usual color changes (compare ref. 10) were observed. After filtration, the solvents were removed *in vacuo* at 40° and the solid residue was taken up in a mixture of 60 cc of ethanol and 3.5 cc of water. This solution was concentrated *in vacuo* to 30 cc and then poured into 280 cc of cold water. The mixture was stored for 2 hours at –10° and the crystalline precipitate was filtered and dried. The methyl Δ^4 -12 α -acetoxy-3-oxo-17 α -methyletiate-3-semicarbazone (IXa) thus obtained (1.227 g) melted with decomposition at 193–196°; $\lambda_{\text{max}}^{\text{EtOH}}$ 270 m μ (log ϵ 4.7).

To a solution of the semicarbazone IXa (1.227 g) in 37 cc of acetic acid and 13.3 cc of water, 3.3 cc of a 1.64 *N* aqueous pyruvic acid solution was added. The mixture was flushed with carbon dioxide and the flask was sealed. After 19 hours the product was poured into 300 cc of ice water and the precipitate was extracted with ether. The organic

solution was washed with cold sodium carbonate solution, with iced dilute hydrochloric acid, with bicarbonate solution, and with water, and was then dried over sodium sulphate. Removal of the solvent afforded 1.104 g (96.9% yield from VIIIa) of methyl Δ^4 -12 α -acetoxy-3-oxo-17 α -methyletienate (IX), m.p. 164–167.5°. A sample was recrystallized twice from ether–hexane for analysis; colorless needles, m.p. 165.5–167.5°, $[\alpha]_D^{25}$ 242.5° (c, 0.756 in CHCl_3), $\lambda_{\text{max}}^{\text{EtOH}}$ 239 m μ (log ϵ 4.46). Anal. Calc. for $\text{C}_{24}\text{H}_{34}\text{O}_5$: C, 71.61; H, 8.51. Found: C, 71.56; H, 8.42.

(b) In another series of experiments, 3.59 g of the acetoxy keto ester VIII was transformed in a similar manner to 4.457 g of crude bromide VIIIa which afforded, upon crystallization from ether–methanol, 2.41 g of pure bromo ketone VIIIa, m.p. 181–183°. This bromide was transformed, as described above, to 2.424 g of semicarbazone IXa, m.p. 186–194° decomp., which gave upon hydrolysis with aqueous acetic acid and pyruvic acid (compare above) 1.934 g of the 4-unsaturated ester IX, m.p. 164–166°. The mother liquors from the crystallization of the crude bromide (2.043 g) were treated in the same way as the pure bromide. Purification by chromatography and recrystallization of the resulting Δ^4 -3-ketonic material gave 1.106 g of slightly less pure ester IX, m.p. 157–163°. In this run the total yield of the transformation of the saturated ester VIII to the unsaturated ester IX amounted to 85.1%.

Methyl $\Delta^{3,5}$ -3-Ethoxy-12 α -acetoxy-17 α -methyletiadienate (XII)

By the procedure described by Julian and co-workers (17), 1.934 g of the Δ^4 -3-keto ester IX was transformed to the enol ether XII. Recrystallization of the crude crystalline reaction product from acetone–methanol in the presence of traces of pyridine gave 1.428 g (69%) of beautiful needles, m.p. 180.5–182°. From the mother liquors, 119 mg (5.8%) of a product of lesser purity, m.p. 169–173°, was isolated. A sample was recrystallized four times for analysis; m.p. 183–184.5°, $[\alpha]_D^{24}$ –12.2° (c, 1.04 in pyridine), $\lambda_{\text{max}}^{\text{EtOH}}$ 240 m μ (log ϵ 4.4). Anal. Calc. for $\text{C}_{26}\text{H}_{38}\text{O}_5$: C, 72.52; H, 8.90. Found: C, 72.71; H, 9.03.

Hydrolysis

A sample of 65 mg of enol ether XII was dissolved in 5 cc of acetone and treated for 12 hours, at room temperature, with 1 cc of 2 *N* hydrochloric acid. Ether extraction gave an amorphous product which yielded, after crystallization from ether–hexane, 32 mg of the Δ^4 -3-keto ester IX, m.p. 166.5–168.5°, not depressed upon admixture of an authentic sample.

Δ^4 -12 α -Hydroxy-3-oxo-17 α -methyletienic Acid (XI)

(a) In a sealed tube, 1.428 g of enol ether XII was heated for 48 hours to 169° with 60 cc of a 6.9% methanolic potassium hydroxide solution. The product was cooled, diluted with 400 cc of water, and acidified with 40 cc of 2 *N* sulphuric acid. Filtration of the precipitate afforded 1.063 g of a crude product which melted between 192.5 and 196.5°. Repeated crystallization from acetone afforded 808 mg (70.3% yield) of Δ^4 -3-keto acid XI, m.p. 274–280°. The product was recrystallized for analysis; short, fine needles, m.p. 277–280°, $[\alpha]_D^{25}$ 123° (c, 0.934 in methyl cellosolve). Anal. Calc. for $\text{C}_{21}\text{H}_{30}\text{O}_4$: C, 72.80; H, 8.73. Found: C, 72.70; H, 8.67.

(b) In another run, 705 mg of enol ether XII was saponified as described under (a). The reaction product was acidified with concentrated hydrochloric acid and the mixture was diluted with chloroform. The product was kept for 30 minutes at room temperature, with repeated shaking. Subsequently, the organic solution was washed until neutral and the solvent was removed. Thus 520 mg (91.7% yield) of acid XI, m.p. 272.5–276°, was obtained.

Remethylation and Reacetylation

A solution of 60 mg of the hydroxy keto acid XI, m.p. 275–277°, in 10 cc of absolute methanol was treated at 0° with 15 cc of a 2% ethereal diazomethane solution. The mixture was stored for 8 hours at 0° and the solvents were removed *in vacuo*. The crude reaction product was dissolved in 5 cc of pyridine and refluxed for 90 minutes with 2.5 cc of acetic anhydride. The usual working up gave 96 mg of an oil which was chromatographed on 2.5 g of aluminum oxide. Petroleum ether – benzene (1:1, 1:4), benzene, and benzene–ether (4:1) eluted 71 mg of acetoxy keto ester IX, m.p. 155–162°. Recrystallization raised the melting point to 163–166°; the melting point was not depressed upon admixture of authentic ester IX.

Methyl Δ^5 -3-Ethylenedioxy-12 α -acetoxy-17 α -methyletlenate (X)

A solution of 2.759 g of methyl Δ^4 -12 α -acetoxy-3-oxo-17 α -methyletlenate (IX), m.p. 162.5–165°, in 206 cc of absolute benzene was reduced to 150 cc. Freshly distilled ethylene glycol (40.6 cc) and *p*-toluenesulphonic acid (112 mg) were added. The mixture was refluxed for 13.5 hours, with exclusion of moisture and with repeated removal of moist benzene. The reaction product was cooled and poured into an iced, saturated sodium bicarbonate solution, and the precipitate was extracted with ether. The organic solution was washed with 1% sodium carbonate solution and with water and was dried over sodium sulphate. Upon removal of the solvent, 3.02 g (98.7% yield) of ketal ester X, m.p. 176–180°, was obtained. The product was recrystallized twice from ether–hexane for analysis; colorless needles, m.p. 181.5–183°, $[\alpha]_D^{25}$ 51.9° (*c*, 0.847 in CHCl_3). Anal. Calc. for $\text{C}_{26}\text{H}_{38}\text{O}_6$: C, 69.92; H, 8.58. Found: C, 69.92; H, 8.66.

Δ^5 -12 α -Hydroxy-3-ethylenedioxy-17 α -methyletlenic Acid (XIII)

In a sealed tube, 4.984 g of acetoxy ketal ester X, m.p. 177–180°, was treated for 48 hours with 102 cc of a 6.8% methanolic potassium hydroxide solution at 170°. The reaction product was poured into 1 l. of water and the mixture was extracted with ether. The usual working up of the ethereal solution gave 7 mg of an amorphous product. The aqueous alkaline solution was carefully acidified with 1 *N* sulphuric acid to the congo blue reaction, and the mixture was extracted with chloroform. The organic solution was washed until neutral and then dried over sodium sulphate. Removal of the solvent afforded 4.49 g of a crystalline residue which gave, upon recrystallization from ether–methanol, 3.572 g of acid XIII, m.p. 125–130°/209–212°, and a second crop of 471 mg, m.p. 125–130°/207–209° (yield of recrystallized product 93%). A sample was recrystallized four times from ether–methanol for analysis; plates, m.p. 211–214°, $[\alpha]_D^{26}$ –10° (*c*, 0.700 in CHCl_3). Anal. Calc. for $\text{C}_{23}\text{H}_{34}\text{O}_6$: C, 70.74; H, 8.78. Found: C, 70.82; H, 8.59.

Δ^5 -12 α -Acetoxy-3-ethylenedioxy-17 α -methyletlenic Acid (XV)

A solution of 513 mg of the hydroxy ketal acid XIII, in 9 cc of pyridine and 4.5 cc of acetic anhydride, was refluxed for 1.5 hours. After the solution had been cooled, 30 cc of ice water was added and the mixture was allowed to stand for 30 minutes. Subsequently, it was diluted with another 200 cc of ice water and shaken repeatedly during 15 minutes. Extraction with ether afforded 566 mg of crude crystalline Δ^5 -12 α -acetoxy-3-ethylenedioxy-17 α -methyletlenic acid anhydride (XIV), which was dissolved in 30 cc of methanol and 7 cc of benzene. A solution of 750 mg of potassium carbonate in 5 cc of water was added and the mixture was refluxed for 1 hour. After dilution with 300 cc of ice water and extraction with ether, the remaining aqueous alkaline solution was carefully acidified in the cold with 0.5 *N* sulphuric acid to give a congo blue reaction. The mixture was extracted

with ether and the organic solution was washed until neutral and dried over sodium sulphate. Removal of the solvent gave 558 mg (98.2% yield) of crystalline Δ^5 -12 α -acetoxy-3-ethylenedioxy-17 α -methyletlenic acid (XV), m.p. 223–224.5°. A sample was recrystallized four times from methylene chloride – hexane for analysis; very fine, short needles, m.p. 231.5–233.5°, $[\alpha]_D^{25}$ 39.8° (c, 0.775 in CHCl_3). Anal. Calc. for $\text{C}_{25}\text{H}_{36}\text{O}_6$: C, 69.42; H, 8.39. Found: C, 69.70; H, 8.44.

Δ^4 -12 α -Acetoxy-17 α -methylpregnene-3,20-dione (VIIId)

At 0°, a solution of 4.05 cc of oxalyl chloride in 19.3 cc of absolute benzene was added dropwise to a suspension of 513 mg of well-dried Δ^5 -12 α -acetoxy-3-ethylenedioxy-17 α -methyletlenic acid (XV) in 23 cc of absolute benzene. During the addition, which took 5 minutes, the flask was shaken vigorously. The agitation was continued for another 30 minutes at room temperature, and subsequently the solvent was removed *in vacuo* at 20–30°. The residue was redissolved in absolute benzene and taken to dryness *in vacuo*; this operation was repeated twice in order to rid the compound completely of oxalyl chloride. The product showed a strong absorption at 240 $\text{m}\mu$ and represented crude Δ^4 -12 α -acetoxy-3-oxo-17 α -methyletlenic acid chloride (XVI). A solution of this chloride in 25 cc of absolute ether and 5 cc of absolute benzene was added, with stirring, to an ethereal solution of dimethyl cadmium prepared, as previously described (2), from 1.29 g of magnesium, 5.3 g of cadmium chloride, and the amounts of methyl bromide and ether equivalent to those used in previous experiments (2). The mixture was refluxed for 1 hour and the excess dimethyl cadmium was destroyed by careful addition of a 10% acetic acid solution. The product was extracted with ether and the ethereal solution was washed with cold, dilute sulphuric acid, with cold sodium bicarbonate solution, and with water, and was then dried over sodium sulphate. Removal of the solvent afforded 397 mg (86.6%) of crude crystalline Δ^4 -12 α -acetoxy-17 α -methylpregnene-3,20-dione (VIIId), m.p. 162–171°, $\lambda_{\text{max}}^{\text{EtOH}}$ 239 $\text{m}\mu$ (log ϵ 4). Recrystallization from ether–hexane raised the melting point to 177.5–183.5°. The analytical sample was prepared by three further recrystallizations from methylene chloride – hexane, from ether–methanol, and finally from pure methanol; colorless prisms, m.p. 189–190°, $[\alpha]_D^{25}$ 165° (c, 0.809 in CHCl_3), $\lambda_{\text{max}}^{\text{EtOH}}$ 240 $\text{m}\mu$ (log ϵ 4.2); $\nu_{\text{max}}^{\text{KBr}}$ 1722 and 1248 cm^{-1} (12 α -acetate), 1690 cm^{-1} (17-methyl-20-ketone), 1667 and 1616 cm^{-1} (Δ^4 -3-keto doublet). Anal. Calc. for $\text{C}_{24}\text{H}_{34}\text{O}_4$: C, 74.58; H, 8.87. Found: C, 74.55; H, 8.92.

Δ^5 -12 α -Acetoxy-3-ethylenedioxy-17 α -methylpregnene-20-one (XVIIIa)

(a) From Δ^5 -12 α -Acetoxy-3-ethylenedioxy-17 α -methyletlenic Acid (XV)

A quantity of Δ^5 -12 α -acetoxy-3-ethylenedioxy-17 α -methyletlenic acid (XV) was dried by repeated evaporation of its benzene solution and by subsequent prolonged heating to 130° in high vacuum. A portion of 2.73 g of this product was suspended in 124 cc of absolute benzene. A solution of 21.6 cc of oxalyl chloride in 103 cc of absolute benzene was added dropwise and with agitation, at 0°, within 5 minutes. The agitation was continued for another 25 minutes. Subsequently, the resulting clear solution was allowed to stand for 30 minutes at room temperature and the product was taken to dryness *in vacuo* at 20–30°. The residue was further dried by repeated evaporation *in vacuo* of its benzene solution and by being kept for 18 hours in high vacuum. The resulting product, which was practically transparent to ultraviolet light in the region of 240 $\text{m}\mu$, and which represented Δ^5 -12 α -acetoxy-3-ethylenedioxy-17 α -methyletlenic acid chloride (XVa), was dissolved in 134 cc of absolute ether. This solution was added, as described above for the preparation of the diketone VIIId, to an ethereal dimethyl cadmium solution prepared from 6.96 g

of magnesium, 29 g of cadmium chloride, and the quantities of methyl bromide and ether equivalent to those used in previous experiments (2). The mixture was refluxed for 1 hour and worked up in the usual way. Thus 2.762 g of a crystalline solid, melting between 115 and 140°, was obtained. The product was filtered over aluminum oxide. The crystalline fractions eluted with ether (2.174 g) were recrystallized from ether-hexane to give 822 mg of a substance melting between 137 and 147°. Further recrystallization from ether-hexane gave 254 mg (10.4%) of pure Δ^4 -12 α -acetoxy-17 α -methylpregnene-3,20-dione (VIIId), m.p. 184–188°, identified by mixed melting point and infrared analysis.

The mother liquors of the first crystallization of this product weighed 1.312 g (48.3%) and crystallized readily from methanol; after one recrystallization they melted at 163–166° and showed, in the ultraviolet, no absorption maximum typical of an α,β -unsaturated ketone.

The methanol fraction of the aluminum oxide filtration (849 mg) was filtered again over aluminum oxide. The resulting crystalline fraction eluted with ether was combined with the crystalline mother liquors of the diketone VIIId, showing no ultraviolet absorption in the 240 $m\mu$ region (see above), and with mother liquors of further recrystallizations of the unsaturated diketone VIIId. This product (1.8 g, 73.8%), representing crude ketal XVIIIa contaminated with some Δ^4 -3-keto derivative VIIId, was chromatographed on 54 g of aluminum oxide (pH 8.5). Petroleum ether-benzene mixtures, benzene, and benzene-ether mixtures eluted 1.104 g (45.3%) of purified Δ^5 -12 α -acetoxy-3-ethylenedioxy-17 α -methylpregnene-20-one (XVIIIa), melting between 159 and 170°. The majority of the fractions melted between 168 and 171°. A sample was recrystallized four times from ether-hexane for analysis; small, fine needles, m.p. 171–172°, $[\alpha]_D^{25}$ 36° (c, 1.055 in CHCl_3). Anal. Calc. for $\text{C}_{26}\text{H}_{38}\text{O}_5$: C, 72.52; H, 8.90. Found: C, 72.40; H, 8.92.

(b) From Δ^4 -12 α -Acetoxy-17 α -methylpregnene-3,20-dione (VIIId)

A solution of 254 mg of the Δ^4 -3,20-diketo acetate VIIId in 310 cc of absolute benzene was refluxed for 3 hours with 8 cc of ethylene glycol and 22 mg of *p*-toluenesulphonic acid. During this period the mixture was stirred vigorously and the moist benzene was removed periodically by the use of a water trap. The usual working up afforded 294 mg of a product which crystallized upon trituration with methanol; m.p. 132–140°. Recrystallization from ether-hexane gave 94 mg (33.1%) of monoketal XVIIIa, m.p. 164–166°, not depressed upon admixture of authentic 3-monoketal XVIIIa. The mother liquors were chromatographed on aluminum oxide. Petroleum ether-benzene (1:1) eluted 11 mg of a product (m.p. 168–170°) which showed no ketonic absorption in the infrared and to which the structure of Δ^4 -12 α -acetoxy-3,20-bisethylenedioxy-17 α -methylpregnene is tentatively assigned. Further elutions with petroleum ether-benzene gave 54 mg of authentic monoketal XVIIIa, m.p. 158–161° (total yield of monoketal XVIIIa from diketone VIIId: 52.4%).

Δ^5 -12 α -Hydroxy-3-ethylenedioxy-17 α -methylpregnene-20-one (XVIII)

A solution of 239 mg of the 12 α -acetoxy monoketal XVIIIa, m.p. 164–167°, in 15 cc of 6.6% methanolic potassium hydroxide was refluxed for 4 hours. The product was cooled and poured into cold water, the precipitate was extracted with ether, and the ethereal solution was washed until neutral and dried over sodium sulphate. Evaporation of the solvent afforded 215 mg (99.7%) of a product which crystallized upon addition of a drop of hexane; m.p. 172.5–173.5°. A sample was recrystallized three times from ether-hexane for analysis; colorless prisms, m.p. 174.5–175.5°, $[\alpha]_D^{25}$ -23.8° (c, 0.875 in CHCl_3); $\nu_{\text{max}}^{\text{KBr}}$ 3525 cm^{-1} (12-hydroxy), 1684 cm^{-1} (17-methyl-20-ketone)

1102 cm^{-1} (ketal). Anal. Calc. for $\text{C}_{24}\text{H}_{36}\text{O}_4$: C, 74.20; H, 9.34. Found: C, 74.31; H, 9.19.

Δ^8 -12 α -Tosyloxy-3-ethylenedioxy-17 α -methylpregnene-20-one (XVIIIb)

To a solution of 221 mg of hydroxy ketal XVIII, m.p. 164–167°, in 2.6 cc of absolute pyridine, 332 mg of *p*-toluenesulphonyl chloride, m.p. 67–69°, was added. The flask was flushed with nitrogen and sealed, and the mixture was heated for 14 days to 55°. The product was cooled and poured into 100 cc of an ice-cold, saturated sodium bicarbonate solution containing 10 cc of pyridine. This mixture was shaken for 1 hour at room temperature. Subsequently, the product was extracted with ether. The ethereal solution was washed with cold sodium bicarbonate solution and with water and was dried over sodium sulphate. Removal of the solvent *in vacuo* gave 242 mg (78.4%) of a product which crystallized upon addition of a drop of methanol; m.p. 129–131°, $\lambda_{\text{max}}^{\text{EtOH}}$ 225 μ ($\log \epsilon$ 4.1). One recrystallization from methylene chloride – methanol raised the melting point to 135–137°, a second recrystallization, to 140–141°; $[\alpha]_{\text{D}}^{25}$ –10.1° (*c*, 0.957 in CHCl_3). For the subsequent experiment crude crystalline tosylate XVIIIb was used.

$\Delta^{4,11}$ -17 α -Methylpregnadiene-3,20-dione (11-Dehydro-17 α -methylprogesterone) (I)

A quantity of 198 mg of crude tosyloxy ketal XVIIIb was dissolved in a small quantity of benzene and absorbed on 40 g of aluminum oxide (activity 1, pH 8). The column was drained and then heated for 6 hours to 45°. The column was allowed to cool, and elutions with benzene – petroleum ether (4:1) were made; they afforded 100 mg of crude crystalline *Δ^8 -11-3-ethylenedioxy-17 α -methylpregnadiene-20-one (XVII)*, m.p. 167–174°, giving a positive tetranitromethane test. Chromatography of the non-crystalline fractions, under similar conditions, yielded another 13 mg of the same product (total yield: 83.6%). Purification afforded 69 mg (60% yield) of purified ketal XVII, m.p. 171–174°. A solution of this product (69 mg) and of 22 mg of *p*-toluenesulphonic acid in 17 cc of absolute acetone was allowed to stand for 42 hours in a carbon dioxide atmosphere. Ice and aqueous potassium bicarbonate solution were added and the precipitate was extracted with ether. The ethereal solution was washed with potassium bicarbonate and sodium carbonate solutions and with water, was dried over sodium sulphate, and was taken to dryness. The resulting crude crystalline *$\Delta^{4,11}$ -17 α -methylpregnadiene-3,20-dione (11-dehydro-17 α -methylprogesterone) (I)* weighed 58 mg and was purified by chromatography on aluminum oxide. Thus 37 mg of pure, authentic 11-dehydro-17 α -methylprogesterone (I), m.p. 125–139°, was obtained. One further chromatographic purification gave a product melting at 137–138°.

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METAL OXIDE ALKOXIDE POLYMERS

PART II. THE HYDROLYSIS OF TANTALUM PENTAETHOXIDE^{1,2}

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ABSTRACT

The hydrolysis of tantalum pentaethoxide has been studied in boiling benzene and in boiling ethanol. Soluble tantalum oxide ethoxides were obtained over a considerable range of hydrolysis. Infrared studies suggest that Ta—OH groups are absent in these products. Ebulliometric studies have shown that the number-average degree of polymerization varies with the degree of hydrolysis in a characteristic manner and this has been quantitatively explained in terms of fundamental structural models based on octahedrally 6-co-ordinated tantalum.

INTRODUCTION

Recent work on the hydrolysis of titanium (1, 2) and zirconium (3) alkoxides has revealed that some of the metal oxide alkoxide polymers conform reasonably well to structural models based on the 6-co-ordinated metal. In these inorganic macromolecules, polymerization is based on two fundamental processes, namely "condensation" involving M·O·M bridges and co-ordination involving intermolecular metal-oxygen bonds. The previous work in this field (1, 2, 3) has involved the quadrivalent states of titanium and zirconium but the fundamental principles mentioned above should make the structural theory applicable to metals in other valence states. Tantalum forms a pentaethoxide which is essentially dimeric $Ta_2(OEt)_{10}$ (4) and is believed to involve 6-co-ordinated tantalum. Assuming this to be true it seemed that the polymeric tantalum oxide ethoxides $TaO_x(OEt)_{6-2x}$ should provide a good test for the aforementioned structural theory. In particular the system should be considerably simpler from the structural point of view than the titanium and zirconium compounds because the number of possible solvated species is fewer and there should be less possibility of ambiguity in the interpretation of the results. Accordingly, we have made a detailed investigation, mainly by the ebulliometric technique, of the hydrolysis of tantalum pentaethoxide under rigorously controlled conditions.

EXPERIMENTAL AND RESULTS

Tantalum Pentaethoxide

The compound was prepared by the previously described method (4) involving the reaction of $TaCl_5$ with ethanol and anhydrous ammonia in benzene. The $TaCl_5$ was prepared by chlorination of tantalum (99.9% purity metal) at about 400° C. The pentaethoxide (found: Ta, 44.6%; $Ta(OEt)_5$ requires: Ta, 44.6%) was distilled under reduced pressure immediately prior to an experiment and was obtained as a colorless distillate (b.p. 147° C at 0.2 mm).

Ebulliometric Measurements

The technique adopted in this work was similar to that described in our earlier studies (1, 3) and an all-glass ebulliometer involving a differential water thermometer was used.

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Two refinements were developed. One was the use of a silicone-fluid heating bath instead of the flame of a microburner. The heating bath gave steadier ebullition. It was also found that the slight loss of solvent during a long experiment could be obviated by greasing the standard joints of the ebulliometer with a fluorocarbon grease.

Molecular Weight of Tantalum Pentaethoxide in Boiling Ethanol

An accurate knowledge of the degree of polymerization of tantalum pentaethoxide in boiling ethanol was essential for the accurate determination of the degree of polymerization of the tantalum oxide ethoxide produced by hydrolysis in the ebulliometer. Bradley, Wardlaw, and Whitley (4) reported a value of 1.78 compared with 1.98 in boiling benzene. The lower value in boiling ethanol was believed to be due to the presence of a solvated monomeric species, $\text{Ta}(\text{OEt})_5 \cdot \text{EtOH}$, which still involved 6-co-ordinated tantalum. It was important therefore to investigate the degree of polymerization of the pentaethoxide in boiling ethanol over a wide range in concentration since a simple dimer-monomer equilibrium should show a concentration dependence of molecular weight. Five separate determinations were made, each involving several additions of freshly distilled pentaethoxide over the concentration range of approximately 0.01–0.25 g.-mol. (dimer)/1000 g solvent. The method of "internal calibration" (5) using fluorene as standard substance was used. In each experiment there was a linear dependence of the elevation of boiling point with concentration within the probable experimental error of the measurements, and the following values for the degree of polymerization were obtained: 1.85, 1.83, 1.87, 1.81, and 1.88. The mean value of 1.85 was therefore adopted for the degree of polymerization of tantalum pentaethoxide in boiling ethanol. An interesting and puzzling point is the absence of the expected concentration dependence of the molecular weight. The method was quite sensitive enough for detection of a change in degree of polymerization with concentration of the order required by a dimer-monomer equilibrium. It is possible that the system is not in true equilibrium. However, the values obtained in several experiments were quite consistent and it appears that over 90% of the tantalum is present in the dimeric state.

Hydrolysis in Boiling Ethanol

The addition of known quantities of aqueous ethanol (3.70% H_2O , w/w) to boiling ethanolic solutions of tantalum pentaethoxide caused immediate decreases in the elevation of the boiling point due to the increase in degree of polymerization which resulted from the hydrolysis. The correct degree of polymerization of the tantalum oxide ethoxide species was deduced by applying the small correction for the ethanol added with the water. The results of four separate experiments involving different initial concentrations of tantalum ethoxide are recorded in Tables I–IV. The number-average degree of polymerization is denoted by n and the degree of hydrolysis (ratio of moles H_2O added/g.-atom of Ta) by h .

TABLE I
(Expt. 1: initial concn. of $\text{Ta}_2(\text{OEt})_{10} = 0.064$ g.-mol./kg)

h	0.110	0.214	0.321	0.444	0.540	0.634	0.733	0.808	
n	1.94	2.10	2.31	2.58	2.84	3.21	3.50	3.87	
h	0.905	0.992	1.085	1.175	1.27	1.35	1.44	1.55	1.69
n	4.44	5.22	6.08	7.65	8.76	9.21	9.62	9.62	9.94

TABLE II
 (Expt. 2: initial concn. of $Ta_2(OEt)_{10}$ = 0.132 g-mol./kg)

h	0.157	0.355	0.547	0.663	0.702	0.824	0.943	0.996
n	2.02	2.37	2.82	3.14	3.27	3.84	4.51	4.87
h	1.043	1.113	1.17	1.23	1.31	1.37	1.52	1.60
n	5.39	6.00	6.72	7.64	8.59	8.70	9.23	Precipitation

 TABLE III
 (Expt. 3: initial concn. of $Ta_2(OEt)_{10}$ = 0.1525 g-mol./kg)

h	0.101	0.249	0.354	0.451	0.602	0.750	0.910
n	1.94	2.13	2.28	2.49	2.90	3.37	4.01
h	1.02	1.14	1.24	1.35	1.45	1.56	
n	4.66	5.73	7.01	8.30	8.70	Precipitation	

 TABLE IV
 (Expt. 4: initial concn. of $Ta_2(OEt)_{10}$ = 0.2455 g-mol./kg)

h	0.059	0.214	0.294	0.420	0.510	0.576	0.646	0.728
n	1.89	2.07	2.20	2.41	2.62	2.80	2.99	3.29
h	0.822	0.973	1.10	1.24	1.34	1.46	1.59	
n	3.66	4.53	5.41	7.44	9.14	10.2	Precipitation	

Hydrolysis in Benzene

In an attempt to avoid the complications of solvation we determined the degree of polymerization of some tantalum oxide ethoxides in boiling benzene in which tantalum pentaethoxide is dimeric within probable experimental error. The main problem in this aspect of the work is the complete removal of ethanol from the hydrolysis product. The following procedure was believed to be reliable. A known amount of water (as 5% aqueous ethanol) was slowly added with stirring to a known amount (ca. 5 g) of $Ta_2(OEt)_{10}$ in benzene (ca. 100 cc) at room temperature. The solution was then refluxed for $\frac{1}{2}$ hour, allowed to cool under dry nitrogen, and then evaporated at room temperature and 0.1 mm pressure to remove benzene and ethanol. To ensure removal of ethanol the product was redissolved in dry benzene (ca. 50 cc) and the solution again evaporated. This procedure was repeated twice and finally the product was maintained under 0.1 mm at room temperature for about 16 hours. The product was then analyzed for tantalum and ethoxide and its molecular weight was determined ebullioscopically in benzene using the "internal calibration" method involving fluorene. The results are presented in Table V where n_{calc} is obtained by substituting the appropriate value of h in the theoretical equation $n = 6/(3-2h)$ and M is the molecular weight.

TABLE V

h	Found, %		Calc., %		M	n	n_{calc}
	Ta	OEt	Ta	OEt			
0.000	44.6	55.2	44.6	55.4	810	2.00	2.00
0.271	46.8	51.5	46.9	52.1	880, 860	2.27, 2.22	2.44
0.300	47.4	50.5	47.1	51.6	885	2.32	2.50
0.390	47.8	50.0	48.1	50.5	1050, 935	2.77, 2.55	2.70
0.551	49.4	47.5	49.6	48.0	1180	3.22	3.17
0.750	51.8	41.9	52.5	43.7	1510	4.32	4.00

Disproportionation of a Tantalum Oxide Ethoxide

Tantalum ethoxide in benzene, when hydrolyzed to $h = 1.20$ as in the aforementioned manner, gave a gummy oxide ethoxide. (Found: Ta, 57.3; OEt, 36.2. $\text{TaO}_{1.2}(\text{OEt})_{2.6}$ requires: Ta, 57.1; OEt, 37.0%.) This was heated at 290–300° C at 0.01 mm for 3 hours during which time a volatile liquid distilled over and a light brown solid residue remained. (Found: Ta, 78.4%.) The liquid proved to be tantalum pentaethoxide. (Found: Ta, 44.9. $\text{Ta}(\text{OEt})_5$ requires: Ta, 44.6%.) This experiment demonstrated that tantalum oxide ethoxides undergo disproportionation when heated *in vacuo*.

Infrared Spectra of Tantalum Oxide Ethoxides

The absorption spectra of the oxide ethoxides corresponding to $h = 0.55$ and 1.20 were measured in CS_2 solution and compared with the spectrum for tantalum ethoxide. The spectra are too complex to permit a complete interpretation at this stage but it was interesting to find no evidence for hydroxyl bands in the hydrolysis products. Another feature was the steady decrease in intensity of the bands around 3.5 μ , 7 μ , and 18 μ with increase in degree of hydrolysis and these bands presumably involve the ethoxide groups. Simultaneously there was a strengthening of the broad bands in the 19–22 μ region and the appearance of broad, ill-defined bands in the 12–14 μ region. These bands presumably involve the Ta·O·Ta groups. (We are indebted to C. G. Barraclough of University College, London, England, for measuring these spectra.)

DISCUSSION

The hydrolysis of tantalum ethoxide in ethanol was shown by the ebulliometric studies to be an extremely rapid process. The analyses of the products of the hydrolyses carried out in benzene (Table V) and the infrared spectra show that tantalum oxide ethoxides $\text{TaO}_x(\text{OEt})_{5-2x}$ are produced and not tantalum hydroxide ethoxides. Our experiments, under rigorously controlled conditions, have shown that a continuous series of tantalum oxide ethoxides may be produced and that the number-average degree of polymerization increases steadily with the degree of hydrolysis (Tables I–V). Let us now examine these results in the light of the structural theory developed by Bradley, Gaze, and Wardlaw (1, 2) to explain the behavior of titanium oxide alkoxides.

Polymeric Species in Boiling Ethanol

Assuming that tantalum attains octahedral 6-co-ordination in the pentaethoxide, then there are two probable structures, the dimeric unsolvated species (Fig. 1) and the solvated monomer (Fig. 2). These are clearly related to model II (based on $\text{Ti}_2(\text{OR})_8, 2\text{ROH}$)

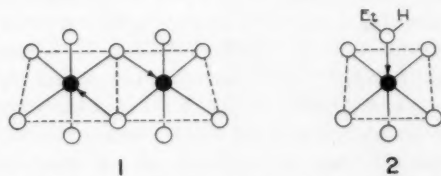


FIG. 1. The dimer $\text{Ta}_2(\text{OEt})_{10}$. ● = Ta, ○ = oxygen in OEt (Et groups omitted).

FIG. 2. The solvated monomer $\text{Ta}(\text{OEt})_5 \cdot \text{EtOH}$. ● = Ta, ○ = oxygen in OEt (Et groups omitted).

and model III (based on $\text{Ti}(\text{OR})_4, 2\text{ROH}$) respectively in the titanium tetraalkoxide structures. If the tantalum pentaethoxide were entirely dimeric in boiling ethanol we should predict that the tantalum oxide ethoxides would conform to a structural series

based on model II for which $n = 6/(3-2h)$ but which have the general formula $Ta_{2(x+1)}O_{3x}(OEt)_{2(2x+5)}$, where $x = 0, 1, 2, 3 \dots \infty$. The limiting bilinear polymer would thus be $[Ta_2O_3(OEt)_4]_{\infty}$ (Fig. 3) corresponding to $h = 1.5$. If the pentaethoxide were entirely monomeric its hydrolysis products might be expected to conform to the analogue of model III for which $n = 3/(3-h)$, and whose formulae would be given by $Ta_{(x+1)}O_{3x}(OEt)_{(5-x)}(EtOH)_{(x+1)}$. We note that the ultimate polymer in this series ($x = 5$, Fig. 4) corresponds to a hypothetical solvated form of tantalum pentoxide. The

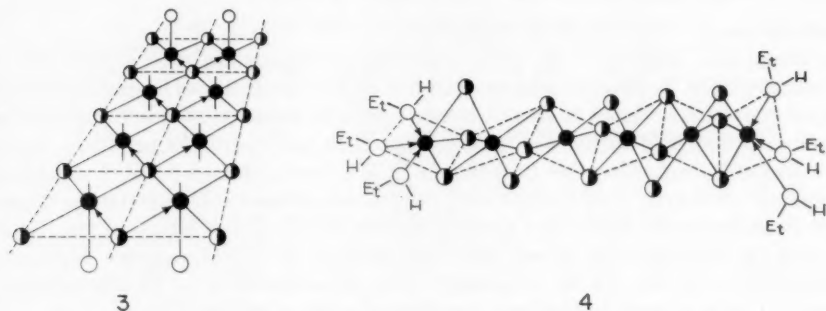


FIG. 3. The infinite polymer $[Ta_2O_3(OEt)_4]_{\infty}$. \bullet = Ta, \circ = oxygen in OEt (Et groups and some OEt groups omitted), \odot = oxygen in Ta-O-Ta groups.

FIG. 4. The hexamer $Ta_6O_{15}(EtOH)_6$. \bullet = Ta, \odot = oxygen in Ta-O-Ta groups.

molecular-weight studies in boiling ethanol showed that the number-average degree of polymerization of tantalum pentaethoxide was 1.85 ± 0.035 and it is thus reasonable to propose that the tantalum oxide ethoxides should exhibit a dependence of number-average degree of polymerization on degree of hydrolysis rather close to the predictions of model II. In Fig. 5 is shown the variation of n with h for all the data included in Tables I-IV in comparison with the theoretical curves for the model II and model III systems. The experimental points are close to the theoretical curve II for $h = 0-1.3$ but deviate at $h > 1.3$ towards curve III. It must be remembered that for the relation $n = 6/(3-h)$ the value of n becomes very sensitive to errors in h at values of $h > 1.0$. For example, at $h = 0.5$ an error of 10% in h would result in an error of only 5% in n , but at $h = 1.0$ a 10% error in h causes a 25% error in n , whilst at $h = 1.25$ a 10% error in h causes a 100% error in n . Hence it is not surprising to find greater scatter in the experimental points at the higher values of h . There is the added factor that the probable experimental error in measuring n is greater at the higher values of n . If we rearrange the expression $n = 6/(3-2h)$ to $1/n = 0.5000 - 0.3333h$, it follows that a plot of $1/n$ versus h should be linear. Similarly the equation representing the theoretical curve III may be transformed to $1/n = 1.0000 - 0.3333h$. It is easily shown that in any system involving, simultaneously, models II and III with a constant value for α_{11} (the proportion of metal atoms in model II), then an equation of the form $1/n = 1.0000 - 0.5\alpha_{11} - 0.3333h$ should be obeyed. We have taken all of the experimental data for $h = 0-1.270$ and determined by the method of least squares the best straight line for the plot of $1/n$ versus h . The results are shown in Fig. 6 where the straight line represents the least-squares equation $1/n = 0.5458 - 0.3389h$. Assuming that values of h are correct, the coefficient of variation for errors in n is $\pm 4.5\%$ and there are 30 changes in sign in the errors when the 52 results are arranged in ascending order of h . The errors are, of course,

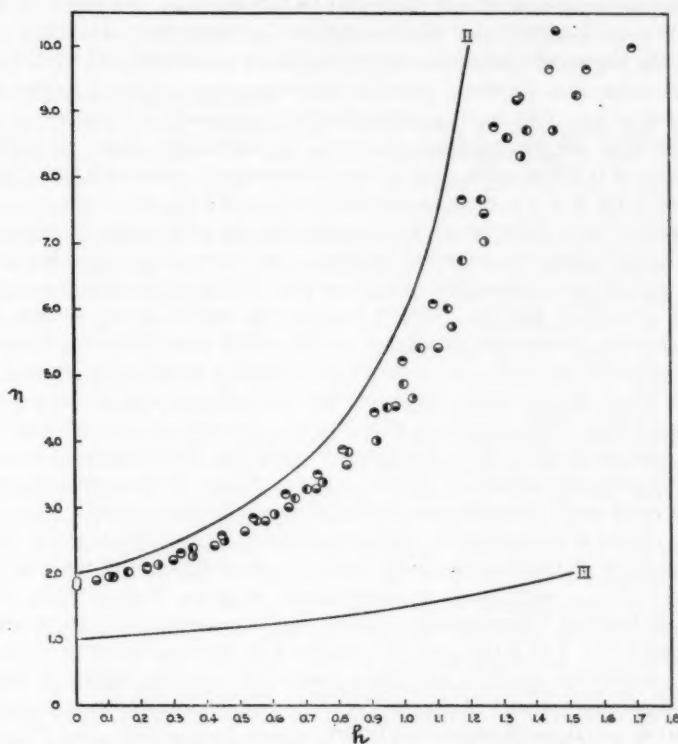


FIG. 5. The variation of η with h for tantalum oxide ethoxides in boiling ethanol. \circ = data from expt. 1, \bullet = data from expt. 2, \odot = data from expt. 3, \otimes = data from expt. 4.

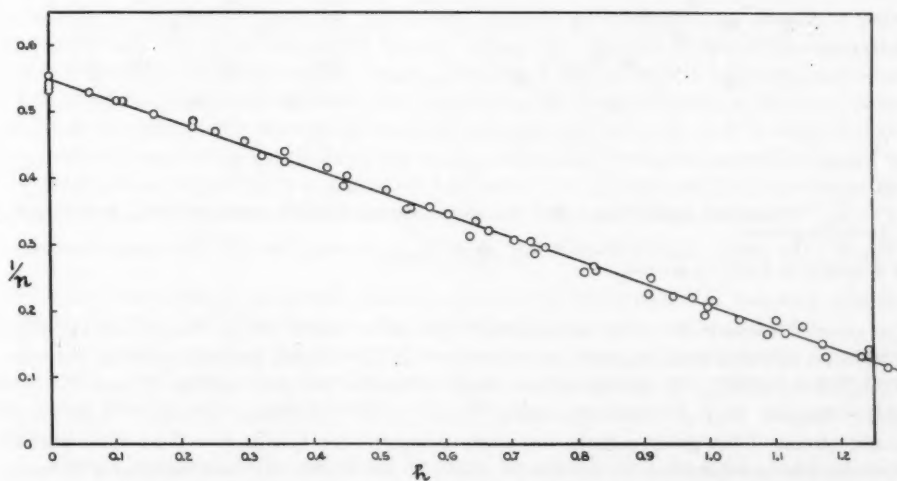


FIG. 6. The plot of $1/\eta$ versus h for tantalum oxide ethoxides in boiling ethanol.

higher at the higher values of h and the coefficient of variation for the first 24 points ($h = 0-0.602$) is only $\pm 1.76\%$ and this is slightly less than the percentage deviation in determining the degree of polymerization of tantalum pentaethoxide. It is interesting to note that the value of α_{II} derived from our least-squares equation is 0.908 and corresponds to a value of $n = 1.83$ for the pentaethoxide compared with the value $n = 1.85 \pm 0.035$ obtained from the five experiments on the pentaethoxide alone. In addition, the least-squares slope of 0.339 is quite close to the "theoretical" value of 0.333. The experimental values of n for $h > 1.3$ show increasing deviations from n_{calc} with increase in h . This may correspond to a decrease in α_{II} as solvation becomes more developed at the lower molar concentrations of polymers, although we cannot rule out the alternative possibility that hydrolysis is incomplete at high values of h due to the presence of relatively stable Ta—OH groups in solution. Before leaving the ebulliometric studies, mention must be made of some alternative structural models which have been considered for the tantalum oxide ethoxide polymers. In model II the repeating units in the bilinear polymer (Fig. 3) involve three oxygen atoms bridging four tantalum atoms along the common edge of four octahedra. This results in the unusual example of a quaternary oxygen bonded to four tantalums in a plane. However, by allowing dimer units to be joined by three oxygens between two tantalums sharing a common face of two octahedra we arrive at another structural model having exactly the same variation of n with h as model II. The alternative model is illustrated by the structure for $Ta_6O_6(OEt)_{18}$ shown in Fig. 7. A zigzag arrangement of the dimers would result in the formation of an infinite linear polymer $[Ta_2O_3(OEt)_4]_{\infty}$ containing no quaternary oxygens. Our present technique cannot distinguish between these two alternatives. We have also considered an alternative to structural model III. The latter may be criticized in having, in some of its species, tantalum atoms which are formally exhibiting oxidation numbers higher or lower than five although the average valency is always five. This problem may be averted by causing the octahedra to share edges as illustrated by the trimer $Ta_3O_4(OEt)_7(EtOH)_3$ (Fig. 8).

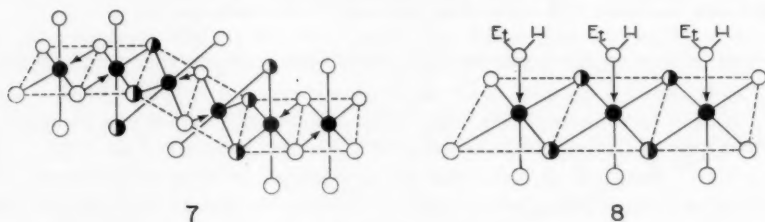


FIG. 7. The hexamer $Ta_6O_6(OEt)_{18}$. \bullet = Ta, \circ = oxygen in OEt (Et groups omitted), \odot = oxygen in Ta \cdot O \cdot Ta groups.

FIG. 8. The trimer $Ta_3O_4(OEt)_7(EtOH)_3$. \bullet = Ta, \circ = oxygen in OEt (Et groups omitted), \odot = oxygen in Ta \cdot O \cdot Ta groups.

The general formula for this series, which we term model IV, is $Ta_{2(x+1)}O_{2x}(OEt)_{5+x}(EtOH)_{x+1}$ and this leads to a new equation: $n = 2/(2-h)$, and an infinite linear polymer; $[TaO_2(OEt)EtOH]_{\infty}$. If the tantalum oxide ethoxides involve models II and IV it is readily shown that a linear equation $1/n = 1.000 - 0.500\alpha_{II} - (0.5000 - 0.1667\alpha_{II})h$ should obtain. This gives exactly the same intercept for $1/n$ at $h = 0$ as the equation given by the combination of models II and III. However, the two equations differ in slope. Using the least-squares value for $\alpha_{II} = 0.908$, a slope of -0.349 is predicted for

the model II - model IV combination compared with the value of -0.333 required by the model II - model III combination. The least-squares value of the slope is -0.339 and this evidently favors the model II - model III system, although the result is hardly decisive.

Insoluble Tantalum Oxide Ethoxides

According to the model II series $n = 6/(3-2h)$, infinite polymers should form as $h \rightarrow 1.5$, whereas for model III the highest possible polymer is the hexamer Ta_6O_{16} , $6EtOH$, and model IV predicts an infinite polymer at $h = 2.0$. Therefore, insoluble products would be expected somewhere in the region $h = 1.5-2.5$. In fact, solution of the least-squares equation $1/n = 0.5458 - 0.3389h$, which satisfactorily described the results up to $h = 1.3$, suggests that n will be infinite at $h = 1.61$. In our ebulliometric experiments we obtained precipitates at $h = 1.60$; at the three higher concentrations of tantalum pentaethoxide, 1.56 and 1.59 , whilst at the lowest concentration no precipitate was formed up to $h = 1.69$. The formation of precipitates in the region of $h \sim 1.6$ is thus reasonable but the presence of species for $h > 1.5$ where model II predicts an infinite polymer requires some comment. If the polymers, even in this region, do conform to models II and III, then soluble species for $h > 1.5$ could obtain if the degree of hydrolysis in model II were less than in model III. This may be illustrated by the following example. Let us imagine that at an over-all average value of $h = 1.55$ the value of α_{II} is 0.8 . Then the polymer equation will be $1/n = 0.6 - h/3$ and for $h = 1.55$ we find $n_{calc} = 12.0$. Now, let us further assume that the average value of h_{II} for the species adopting model II is 1.45 ; this would correspond to $n_{II} = 60$ and these polymers could well be soluble. It follows that if the over-all average h for both species is 1.55 then the average h_{III} for the species in model III must be 1.95 , for which $n_{III} = 2.85$. Finally, it is easily shown that if 80% of the tantalum has an average degree of polymerization $n_{II} = 60$ while the remaining 20% has $n_{III} = 2.85$, then the over-all average value of n is 12 , which is the value predicted from the original equation. Therefore it follows that for all the polymer species to remain soluble at $h > 1.5$, $\alpha_{II} < 1$ and $h_{III} > h_{II}$.

The Molecular Weights of Tantalum Oxide Ethoxides in Benzene

If the tantalum pentaethoxide were not solvated it would be expected to conform exclusively to model II based on the dimer, and the number-average degree of polymerization of the oxide ethoxides would follow the requirements of the equation $1/n = 0.5000 - 0.3333h$. In boiling benzene, tantalum pentaethoxide is dimeric and hence it was important to determine molecular weights of the oxide ethoxides in benzene. Some results at five values of h between 0 and 0.750 are reported in Table V. It is clear that the observed values of n are reasonably close to n_{calc} evaluated from the theoretical equation. The coefficient of variation in n (assuming h is correct) is $\pm 5.5\%$ and this is a satisfactory value, bearing in mind the difficulties mentioned in the experimental section.

CONCLUSIONS

1. The hydrolysis of tantalum pentaethoxide in either ethanol or benzene solution under controlled conditions leads to the formation of polymeric oxide ethoxides.
2. The number-average degree of polymerization of these polymers can be accounted for with the assumption that these compounds are condensation - co-ordination polymers in which the tantalum achieves the co-ordination number of 6 in an octahedral configuration.
3. These octahedral structures are of fundamental significance since they are applicable to either titanium (IV) oxide ethoxides or tantalum (V) oxide ethoxides.

ACKNOWLEDGMENT

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THE REVERSIBILITY OF AROMATIC MERCURATION¹

M. MALAIYANDI, H. SAWATZKY, AND G. F. WRIGHT

ABSTRACT

The ratio of isomeric bisperchloratomercuribenzenes obtained from the monomercurial and mercuric perchlorate in perchloric acid varies slightly with concentration of the acid, but is preponderantly meta. However, more para than meta isomer is obtained under conditions where the para isomer is insoluble in the system. This indicates a mobile equilibrium among the isomers, which is found to extend to all of the polymercuration products. The postulated intermediate for the equilibration, which is 1,2,4-trichloratomercuribenzene, is indicated by the isolation of the similarly oriented 1,2,4,5-perchloratomercuritetrakisbenzene. Although none of the ortho-diperchloratomercuribenzene can be found from this reaction in perchloric acid, it is the principal isomer when phenylmercuric acetate is acetoxymercured neat.

The literature of aromatic mercuration is marked by many inconsistencies. Thus, although Dimroth (1) at 170° C converted mercuric benzoate to anhydro-*o*-hydroxybenzoic acid, an equivalent mixture of benzoic acid and mercuric acetate at 130° C was found to yield the *o*-, *m*-, and *p*-mercured benzoic acids in the ratio 25:57:18 (2). On the other hand, the same equivalence in acetic acid (2.5 hours at 110° C) gave a ratio of 80:20:0 (3).

Several workers have suggested that the discrepancies are due to isomerization. The various results of Table I have in part been explained by Jackson and Frant (2) by the

TABLE I
Mercuration of nitrobenzene

Mercuring agent	Medium	Conditions of reaction	Product ratio			Ref.
			<i>o</i>	<i>p</i>	<i>m</i>	
Hg(OAc) ₂	Nitrobenzene	1:5 by wt. at 150° C until Hg ⁺⁺ test is neg.	58		42	4
		1:5 by wt. at 150° C for 3.5 hr	53	9	38	5
		1:5 by wt. at 95° C for 2.5 hr	57		43	6
		1:5 by wt. at 150° C for 2.5 hr	52		48	6
		1:5 by wt. at 150° C for 2.5 hr	53	15	32	2
		1:2.7 by wt. at 155° C for 2.5 hr	27	6	67	3
Hg(NO ₃) ₂	110 ml 68% HNO ₃	1:2.7 by wt. at 99° C for 7 hr	37	6	56	3
Hg(ClO ₄) ₂	250 ml 60% HClO ₄	1:1.2 by wt. at 23° C for 10 days	11		89	6
	40% HClO ₄ , 250 ml 60% HClO ₄	1:1.2 by wt. at 95° C for 11 hr	37		63	6

possibility that equilibrium is not always attained at once in systems where the mercured nitrobenzenes are not equally stable. Likewise, as is shown for toluene mercuration in Table II, Brown and McGary (9) have suggested that isomerization of the initially

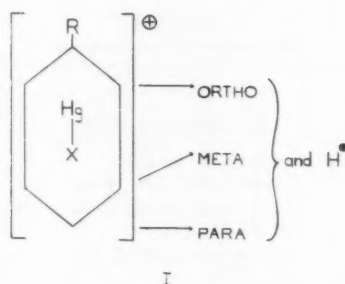
¹Manuscript received February 20, 1961.

Contribution from the Department of Chemistry, University of Toronto, Toronto, Ontario.

TABLE II
 Mercuration of toluene

Reagents			Conditions of reaction		Product ratio			Ref.
Hg(OAc) ₂ , mole	Toluene, mole	Medium, ml	Time, hr	Temp., °C	<i>o</i>	<i>p</i>	<i>m</i>	
0.1	0.1	Neat	5.6	40	43	44	13	7
			5.6	110	43	44	13	6
0.1	0.1	Toluene, 150	1.5	110	41	37	21	6
0.1	0.1	HOAc, 200	6.5	30	17	77	6	6
		HClO ₄ , 10						
0.1	0.1	"	6.5	25	21	67	12	8
0.1	0.1	"	1	25	95	69	21	9
0.1	0.1	"	2	25	40	20	40	9
0.1	0.3	HOAc, 300	ca. 4	50	31	56	13	10
0.1	0.6	"	ca. 4	70	32	53.5	14.5	10
			ca. 4	90	32.5	51.8	15.7	10

formed mercurials seems to be occurring, and that mercuration, like sulphonation (11), is reversible. A similar opinion (12) had been affirmed earlier.



The ionization of mercuric salts is sufficiently incomplete that one may presume aromatic mercuration to involve initially a cationic transition state of appreciable stability. If the decomposition of the intermediate cation is fast, first order, and rate independent of the reaction system, the occurrence of monomercorial isomerization is unexpected, whether or not the reaction is reversible. The intermediate, I, may be expected to be deprotonated along paths related directly with the free energy of the products in the system. Either the activation energy for this final step of mercuration is greater than seems to prevail for other aromatic substitutions or else the isomerization must be related to another mechanism.

Reversible polymercuration provides an alternative path leading to isomerization. Indeed, the substitution of more than one anionomercuri group is so likely that most workers have been troubled by it. Attempts to avoid it (9) are understandable since aromatic polymercurials are difficult to manipulate because of low solubility. Nevertheless, we have deliberately chosen polymercuration of benzene in order to clarify the quandary of variable isomer ratios. By this expedient the directing and the entering group are identical.

At first we started with benzene in aqueous perchloric acid containing mercuric perchlorate. However, we were unable to get consistent results, despite the success of others (13), with this two-phase system. Subsequently we have obtained results that are reproducible by mercuration of mercuric perchlorate with mercuric perchlorate (prepared *in situ* from mercuric oxide) in perchloric acid. The results of a series of experiments in which the water - perchloric acid ratio has been varied are shown in Table III.

TABLE III

Mercuration of 0.0017 mole of phenylmercuric perchlorate with 0.0017 mole of mercuric perchlorate in perchloric acid for 2.5 hours at 25° C

Expt. No.	Perchloric acid		Recovered phenylmercuric perchlorate, %	Yield polymercurated benzenes, %	Isomer, % in polymercurated benzenes		
	Wt. % HClO ₄	Wt. used, g			1,4	1,3	1,3,5
1	50	26	47	46	18	82	Trace
2	50	417	49	10			
3	55	417	60	28	18	82	Trace
4	60	417	17	64	19	81	Trace
5	65	417	12	74	34	62	5
6	70	417	12	77	57	39	3
7	70	670	16	75	28	69	3

The analyses of the products have been accomplished, after solvent-extractive separation of phenylmercuric chloride from the physically intractable benzenepolymercuric chlorides, by quantitative conversion to the polybromobenzenes. The methods used previously (14, 15) have been modified slightly. The distillable dibromobenzenes have been identified by infrared absorption using the intense bands relating to out-of-plane wagging modes. The results have been checked by thermal analyses and by isolation of *m*-dibromophenylchlorophenylsulphonamide when the ortho isomer is absent.

The series of experiments which are outlined in Table III show that in perchloric acid none of the ortho isomer can be detected with certainty. In the more dilute perchloric acid (expts. 1-4 inclusive) the meta isomer is preponderant; there are lesser amounts of para isomer and of symmetrical trimercurated benzene. Since the sum of these polymercurated products together with unchanged phenylmercuric perchlorate does not constitute a quantitative yield one may expect that other polymercurated benzenes, in small amount, have been missed. Also some benzene must have been formed, and lost, if aromatic mercuration is reversible. This reversibility is apparent when 50% perchloric acid is used in large excess as the reaction medium (expt. 2, Table III). The low yield of polymercurials may be contrasted to 4.6 times as much as that obtained from expt. 1. Since separate experiments show that these are equilibrium states which were attained after 150 minutes, and the amount of recovered monomercurial is essentially the same for expts. 1 and 2, the difference must be attributed to the formation of benzene.

In this connection it is of interest that at 25° C the solubility in 50% aqueous perchloric acid of phenylmercuric hydroxide (20 g/l.) is 10 times as great as in 70% perchloric acid. Thus it would appear that the phenylmercuric salt was more highly ionized or hydrated (or both) in the more aqueous medium.

Addition of sodium perchlorate to the reaction systems described in Table III does not alter appreciably either the yields or the isomer ratio of substitution products. Neither does the acid concentration (see expts. 1, 3, and 4) up to a level of 61%, but in the same

amount of more concentrated perchloric acid (expts. 5 and 6) the relative yield of meta isomer decreases. The reason is quite apparent: after 20 minutes from 65% or after 4 minutes from 70% perchloric acid a precipitate appears which is nearly pure 1,4-diperchloratomercuribenzene. The amount of this precipitate increases when the total volume of 70% perchloric acid is decreased, or (expt. 7) much less of the precipitate appears when the volume of the system is greater.

Inspection of Table III shows that when this precipitation occurs (expts. 5 and 6) the meta isomer decreases in quantity and only slightly in favor of some 1,3,5-trimercurial which appears. It would seem that this meta isomer, which may be the initial polymercuriation product, is converted to para isomer which then can precipitate. Indeed, when a system identical with that of expt. 6 is quenched after 4 minutes of reaction time (and before precipitation has commenced), the product contains only 25% of 1,4-bismercurial instead of the 57% obtained after the 150-minute reaction period of expt. 6 during which precipitation occurs. Moreover, the initial formation of the meta isomer must be rapid, because the polymercurial yield after 4 minutes is 60% of that obtained after 150 minutes of reaction time.

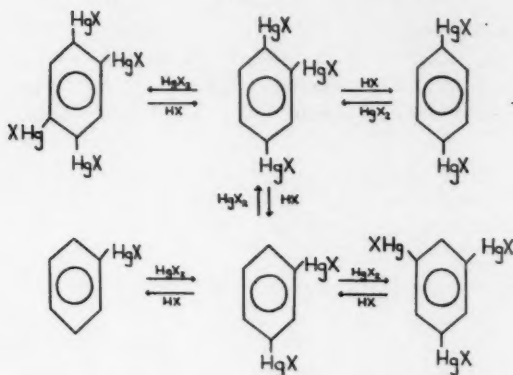
In order to test further the possibility that the meta isomer is the initial perchloratomercuriation product we have prepared 1,3-hydroxymmercuribisbenzene from 1,3-benzenedisulphinic acid and have dissolved it in 70% perchloric acid. After 2 hours the reaction system is drowned with aqueous sodium chloride. Besides a 20% yield of phenylmercuric chloride the mixture has been shown to contain 1,4-chloromercuribisbenzene as well as a small amount of 1,3,5-trimercurial. Thus a profound disproportionation of 1,3-bismercurial has occurred, undoubtedly to give benzene as well.

Except when it precipitates from solution, the 1,4-perchloratomercuribisbenzene is not inert toward the reaction system. When it is treated with a 12 molar excess of mercuric perchlorate in 70% perchloric acid for 2 hours the yield of mono- and di-mercurials is very small. Bromination of the remainder shows that *sym*-trimercurial is the principal product although a 5% yield of 1,2,4,5-tetrabromobenzene indicates the presence of this tetramercurial.

The perchloratomercuritrisbenzene also must not be considered to be an ultimate end product. When it is treated with monoperchloratomercuribenzene in 70% perchloric acid the system, after 2 hours, contains only 40% of the trimercurial while 40% of the two dimercurials has appeared.

On the basis of these findings the mode of reaction given below has been drawn up ($X = \text{ClO}_4$), although one important piece of evidence is lacking. In all of the systems which have been analyzed, the key substance, 1,2,4-tribromobenzene, indicative of the analogous trimercurial, has been sought assiduously, but never found. Despite the fact that the low melting point (44°) of 1,2,4-tribromobenzene makes isolation difficult, we are inclined to attribute the apparent absence of 1,2,4-triperchloratomercuribenzene to its high reactivity. Certainly it cannot be excluded because ortho perchloratomercuriation is involved since the isolation of 1,2,4,5-tetrabromobenzene shows that ortho substitution can occur. Therefore, the transition to and from meta and para dimercurated benzenes seems to be explicable better by postulation of the 1,2,4-trisubstituted intermediate than by simple "isomerization".

The absence of evidence for initial ortho mercuriation in the studies with perchloric acid should not be construed as proof that it does not occur. The perchloratomercuriation of 1,2-perchloratomercuribisbenzene and the alternative reversal from the 1,2,4-trimercurial to 1,3-perchloratomercuribisbenzene may be so rapid that only the appearance



of the latter substance is first observed. However, initial ortho mercuration need not be a necessary condition of the reaction. Meta substitution may be a very rapid reaction, as is observed when phenyltrimethylammonium salts are nitrated to give exclusively the meta nitro compound in high yield (16, 17). No postulation of prior ortho-para substitution can be made in this event since nitration is essentially irreversible.

Actually a preponderance of ortho substitution is observed when phenylmercuric acetate is fused with mercuric acetate at 145–150° C. The reaction does not seem to be amenable to detailed study because of the complication that the acetato group also is mercurated (18) even though a reasonable separation of the mercurated acetic acid can be made (19). Although the yields vary unaccountably between 35 and 50% the ratio of bismercurials, *o*:*m*:*p*, is consistent at 65–66:23.5–24.5:11. An otherwise comparable experiment, in which mercuric acetamide replaces the acetate, yields 43% of bismercurials in *o*:*m*:*p* ratio of 69:18:12.

EXPERIMENTAL

Mercuration of Phenylmercuric Perchlorate

This procedure was used when various concentrations of perchloric acid were compared in mercuration. A sample of phenylmercuric hydroxide (m.p. 226–228° C) (20) weighing 0.50 g (0.0017 mole) was dissolved in perchloric acid (usually 417 ml) of the desired concentration. To this stirred solution at 25° was added 0.37 g (0.0017 mole) of mercuric oxide. The closed system was stirred only gently (to minimize loss of benzene) for 150 minutes.

Subsequently the system was poured into 1 liter of crushed ice, and 20% aqueous sodium hydroxide was added until the mixture was slightly basic. Then 1 g of sodium bromide was added. Acidification with acetic acid produced a precipitate which was allowed to settle while the remainder of the ice was melting. The precipitate was filtered off and washed thoroughly with water to remove soluble salts. Then it was washed with boiling ethanol and boiling benzene to remove phenylmercuric bromide, leaving the insoluble polymercurated benzenes.

p-Chloromercuribisbenzene

Following the procedure outlined above with 70% perchloric acid (d_{20} 1.67, 417 ml) the original system was stirred for 20 minutes. Then 0.05 g (0.00017 mole) of phenylmercuric

hydroxide and 0.037 g (0.00017 mole) of mercuric oxide were added. Subsequently, nine more such additions were made every 20 minutes with continued stirring. Twenty minutes after the last addition the solid was filtered off and dissolved in water, then treated with sodium chloride. The purity of the infusible *p*-chloromercuribisbenzene (0.65 g, 32%) is indicated by the melting point (74–82°) of the *p*-dibromobenzene, which may be prepared from it quantitatively (21).

Treatment of the remainder of the reaction system (the filtrate) with ice and then with sodium bromide yielded 0.56 g of polymercurated benzenes which contained 22% of 1,4-bromomercuribisbenzene according to the prescribed bromination analysis described below.

Isomerization of p-Dimercurated Benzene

The 1,4-perchloratomercuribisbenzene was filtered from a reaction system such as has just been described; it was washed thoroughly with ethanol and then was dried *in vacuo* at 25° C. A mixture of 0.50 g (0.00074 mole) of 1,4-perchloratomercuribisbenzene in 200 ml of 70% perchloric acid containing 0.238 g (0.0011 mole) of mercuric oxide was stirred at 25° C. After 180 minutes the clear solution was drowned and treated as described above to give 0.04 g (17%) of phenylmercuric bromide and 0.40 g (25%) of polymercurated benzenes. Analytical bromination showed that this mixture contained 10% of the *p*-isomer, 57% of the *m*-isomer, and 24% of the 1,3,5-perchloratomercuritrisbenzene.

In a variation of this procedure 0.25 g (0.00037 mole) of 1,4-perchloratomercuribisbenzene in 50 ml of 70% perchloric acid containing 1.00 g (0.0046 mole) of mercuric oxide was stirred at 25° C for 2 hours and then was processed according to the earlier description to remove *p*-isomer (filtration) and then phenylmercuric salt (benzene-ethanol extraction). The remainder (0.31 g) when treated with bromine gave 0.09 g of solid polybromobenzenes. A hot ethanol (2.5 ml) solution, upon cooling, yielded 0.004 g (5%) of 1,2,4,5-tetrabromobenzene, m.p. 165–173° C. After crystallization from ethanol (m.p. 179–180° C) a mixture melting point with an authentic sample (22) was not depressed.

The ethanolic mother liquors were concentrated to yield 0.07 g, m.p. 65–92° C. Crystallization from petroleum ether (b.p. 40–60° C) showed that this material was largely 1,3,5-tribromobenzene, m.p. 118–119° C.

1,3-Chloromercuribisbenzene

A suspension of 4.70 g (0.0238 mole) of *m*-benzenedisulphinic (23) acid in 10 ml of water was made alkaline by addition of 50% aqueous sodium hydroxide and the whole was added to a boiling solution of 16.35 g (0.06 mole) of mercuric chloride in 50 ml of water. A curd appeared after 30 seconds and the system thickened to a paste on the steam bath. After 20 minutes the strongly acidic system was diluted with 50 ml of water and was maintained on the steam bath for 6 hours. The precipitate was filtered off and washed with hot water until free from mercuric salts (of which 0.015 mole was washed out), and then with boiling ethanol and boiling benzene. The remainder weighed 70.7 g or 82% of theoretical. Anal. Calc. for $C_6H_4Hg_2Cl_2$: C, 13.15; H, 0.73. Found: C, 13.0; H, 1.2. Upon treatment with bromine in excess the *m*-dibromobenzene, b.p. 85–90° C (15 mm), which was obtained in 65% yield, was converted to 2,4-dibromobenzene-sulphonyl chloride, m.p. 75–78° C, mixed m.p. not depressed.

1,3-Hydroxymercuribisbenzene

A suspension of 10.7 g (0.0196 mole) of 1,3-chloromercuribisbenzene in 2 liters of 0.65%

aqueous sodium hydroxide was heated to boiling and filtered hot. The filtrate was evaporated to a 200-ml volume and cooled, precipitating 3.76 g (38%) of chlorine-free product. Treatment with bromine according to the procedure described below gave a quantitative yield of pure 1,3-dibromobenzene, b.p. 86–90° C (15 mm), according to freezing point (–2° C) and to the 2,4-dibromobenzenesulphonyl chloride, m.p. 77–78° C, which was derived from it.

Isomerization of 1,3-Perchloratomercuribisbenzene

Some heat is evolved when 0.50 g (0.00096 mole) of 1,3-hydroxymmercuribisbenzene is dissolved in 150 ml of 70% perchloric acid. The solution was cooled to 25° C and let stand for 2 hours and then was drowned in ice, neutralized with alkali, and treated with sodium chloride. Extraction with hot benzene-ethanol removed 0.06 g of phenylmercuric chloride, m.p. 248° C. The alcohol- and benzene-insoluble part (0.36 g) was found by the analytical bromine technique to contain 25% of the *p*-isomer and less than 1% of bromotrisbenzene.

1,3,5-Chloratomercuritrisbenzene

A solution of 0.20 g (0.00068 mole) of phenylmercuric hydroxide in 100 ml of 70% perchloric acid was treated at 25° C with 1.70 g (0.00785 mole) of mercuric oxide. The system became and remained clear, unlike systems without excess of mercuric perchlorate. After 2 hours the system was poured into 2 kg of ice, and 20% aqueous sodium hydroxide was added to slight basicity. Then 1 g of sodium bromide was added, together with sufficient acetic acid for slight acidity. The precipitate, essentially bromomercuritrisbenzene, weighed 0.62 g (100%) and when brominated gave 0.21 g, m.p. 97° C. Crystallization from petroleum ether raised this melting point to 118–119° C; mixed m.p. not lowered.

Demercuration of Chloratomercuritrisbenzene

A quantity of material which was chiefly chloromercuritrisbenzene according to the bromination method of analysis was converted to the hydroxymmercurial by washing it exhaustively with alkali. A suspension of 0.49 g (0.00067 mole) of this hydroxymmercurial with 0.16 g (0.00054 mole) of phenylmercuric hydroxide was stirred with 150 ml of 70% perchloric acid for 3 minutes until the system was homogeneous. After 2 hours the system was drowned and processed as is outlined above. The recovered phenylmercuric chloride and the polymmercurial portion weighed 0.07 g and 0.41 g respectively. Analysis of the latter by the bromination technique showed that 48% was dimercurated benzenes while 52% was trimercurated. This amount of trimercurial is 42% of that originally used, so that at least 58% has been demercrated. Likewise, the recovery of monomercurial is 44% of that first introduced to the system.

Acetoxymercuration of Phenylmercuric Acetate

A finely ground mixture of 10.0 g (0.03 mole) of phenylmercuric acetate and 12.78 g (0.047 mole) of purified mercuric acetate was heated in a large test tube and was immersed in a sulphuric acid bath at 150° C during 30 minutes. The clear melt became quite viscous. The system was allowed to cool gradually, then was finely ground and exhaustively washed with boiling ethanol and benzene to remove 1.2 g of unchanged phenylmercuric acetate. The remainder was washed five times with 200-ml portions of 5% aqueous sodium hydroxide containing 10% sodium bromide. After each washing the material was dried and reground. Finally it was washed with dilute acetic acid and with water. There remained after drying 9.5 g (58%) of infusible solid. Analysis by

the bromination method (spectral analysis) showed that it contained 64.8% ortho, 24.4% meta, and 10.8% para isomer. Duplication gave 65.8% ortho, 23.3 meta, and 10.8 para.

An otherwise identical experiment with mercuric acetamide gave a product with an *o:m:p* ratio of 69.3:18.4:12.3.

Identifications and Analyses

Because of the large atomic weight of mercury, an elemental analysis for carbon is chiefly, and for hydrogen or mercury entirely, meaningless. For this reason the mercurials and mixtures of them that are described in this report have largely been characterized by conversion to brominated benzenes. For a quantity of mercurial not to exceed 0.70 g the following procedure is used.

Bromination of Mercurials

The sample is added to a stirred two-phase system comprised of 5.0 ml of carbon tetrachloride with a solution of 3.0 g of potassium bromide in 15 ml of water. Bromine is added at such a rate that its color is just maintained. When the solid has disappeared the brominated benzenes are in the non-aqueous phase and the mercuric salts are in the aqueous phase.

The non-aqueous phase is vacuum-evaporated and the residue is distilled under 13 mm. The dibromobenzenes distill at 85–87° C while the residue consists of polybromobenzenes, 96–108° C. A single crystallization from 95% ethanol raises this melting point to 118–119° C, not depressed by admixture with 1,3,5-tribromobenzene. Since the weight of the distillation residue is 5% higher than the known amount from a calculated mixture of dibromobenzenes and 1,3,5-tribromobenzene, this residue weight less 5% is taken as presumptive for anionomercuritrisbenzene.

The method of Ferguson and Levant (24) for infrared spectral analysis of chlorobromobenzenes was simplified by use of the same cell for all determinations of 7–10% solutions in carbon disulphide so that optical density instead of extinction coefficient could be employed. The wavenumbers frequencies chosen include the three corresponding (but at lower frequencies) to those chosen by Whiffen *et al.* in their analysis of cresols (25) although the number has been extended (607 and 742 cm^{-1} for ortho; 664, 723, and 765 cm^{-1} for meta; 805 cm^{-1} for para). The optical densities of 12 known mixtures over the entire range of concentrations have been plotted for each frequency. Since these plots are practically linear and there is little overlap of the key frequencies, the percentages of isomer are read directly and (in the case of ortho and meta) averaged for the several frequencies used for these isomers. Although part of the *p*-dibromobenzene may be separated as such (m.p. 85–86° C) by chilling the distilled mixture of dibromobenzenes they are usually analyzed *in toto*.

When the ortho isomer is practically absent a two-component thermal analysis may be made for percentages of the meta and para dibromobenzenes. The hot oil is transferred by means of small capillaries to melting-point tubes about 1 mm in diameter. The disappearance of the last crystal is recorded while the sample is stirred by reciprocal motion of the capillary. The rate of heating is about 1° C per 5 minutes in a thaw-point apparatus (26). The diagram is shown in Fig. 1.

Meta-para mixtures of dibromobenzene also may be analyzed by the method of Huntress and Carten (27) because 1,4-dibromobenzene does not react with chlorosulphonic acid. For example, 0.30 g (0.0012 mole) of dibromobenzenes (from which part of the para isomer had been removed by filtration at 4° C) was treated at 0° C with 2.50 g (0.0215 mole) of chlorosulphonic acid (distilled at 147–149° C in a stream of

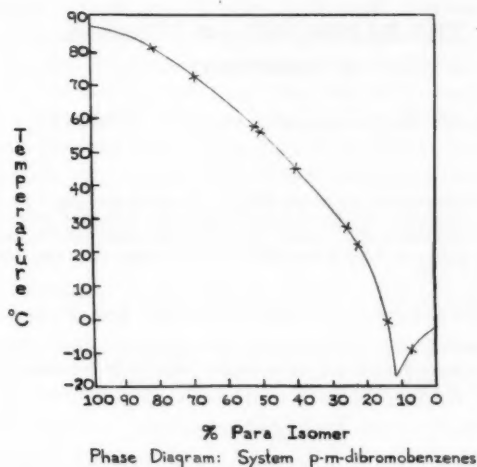


FIG. 1.

hydrogen chloride). After the reaction had subsided the system was warmed and held for 20 minutes at 20–25° C and then was drowned in ice. The white solid, 0.36 g, m.p. 57–73° C, was crystallized from 4 ml of petroleum ether (b.p. 40–60° C), yielding 0.33 g, m.p. 80–82° C, not depressed by admixture with authentic 2,4-dibromobenzenesulphonyl chloride. Refluxing with concentrated ammonia converts this product to 2,4-dibromobenzenesulphonamide, m.p. 189–190° C.

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THE RADIOLYSIS OF ETHANOL

I. VAPOR PHASE¹

J. M. RAMARADHYA² AND G. R. FREEMAN

ABSTRACT

The alpha radiolysis of ethanol vapor at 108° C produced hydrogen as the major single product, with smaller amounts of methane, carbon monoxide, ethylene, ethane, acetaldehyde, formaldehyde, water, 2,3-butanediol, 1,2-propanediol, propanol, and butanol. The initial yield of hydrogen was $G(H_2) = 8.9 \pm 0.4$, which is much higher than the values reported for the liquid phase ($G(H_2) = 4$).

A mechanism is proposed to account for the formation of the products. However, the observed value of $G(H_2O) = 5.4$ is over four times larger than can be explained by the mechanism.

There is a good material balance in the observed reaction products, which indicates that little polymerization occurred during the radiolysis. This is in marked contrast with the vapor phase radiolysis of cyclohexane.

INTRODUCTION

Although the radiolysis of liquid ethanol has been studied using helium ions (1, 2) and Co⁶⁰ gamma rays (3), very little attention has been paid to the vapor phase radiolysis of ethanol. In the liquid phase radiolysis of ethanol, the gaseous products were hydrogen, carbon monoxide, methane, ethylene, and ethane and the liquid products were formaldehyde, acetaldehyde, and vicinal glycols.

One previous study of ethanol vapor by cathode-ray bombardment has been reported by McLennan and Patrick (4). The products reported were hydrogen, carbon monoxide, carbon dioxide, methane, ethane, formaldehyde, and acetaldehyde. In this paper, an investigation of the radiolysis of ethanol vapor by Po²¹⁰ alpha particles is described.

EXPERIMENTAL

The apparatus and the general experimental technique used in this investigation are similar to those described in an earlier paper (5).

The ethanol was from Reliance Chemical Ltd., containing about 0.11 mole% water. Three and one-half grams of sodium was dissolved in 500 ml of ethanol and 14 g of diethyl phthalate was added to the solution (6). This solution was refluxed for 2 hours and was distilled in a system protected from moist air by passing dry hydrogen through it. The hydrogen was dried by passing it through a trap containing silica gel, immersed in liquid nitrogen. Only the middle one-third of the distillate was retained. After the purification the ethanol contained only 0.005 mole% water.

The purified ethanol was degassed and stored under vacuum in a reservoir. Prior to irradiation, 1.6 ml of the ethanol was distilled into a calibrated tube, where its volume was accurately measured at 0° C, and then volatilized into the reaction chamber.

The reaction chamber was a 1-liter bulb, heated to 108° C, containing a nominally 100-mc Po²¹⁰ source (5). The polonium source was calibrated by Fricke dosimetry, using $G(Fe^{+++}) = 5.5$ (5). All the energy of the alpha particles was absorbed by the ethanol vapor during an experiment.

The products of the ethanol vapor radiolysis were analyzed by low-temperature distillation and by gas chromatography. The fraction of gaseous products that was volatile

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at -196°C consisted of hydrogen, carbon monoxide, and methane. It was collected and measured in a McLeod-Toepler apparatus and then analyzed on a 1-m activated charcoal column. Another gaseous fraction, noncondensable at -112°C and consisting of residual methane and C_2 , C_3 , and trace amounts of C_4 hydrocarbons, was analyzed using a 2.5-m silica gel column. The analyses of the various liquid products were performed using 2.5-m carbowax 1500, 2.5-m didecyl phthalate, and 1-m ucon columns.

Anhydrous ethanol is very hygroscopic. Water was also a reaction product. When the yield of water was being determined, samples of unirradiated ethanol were put through the entire analytical procedure and then analyzed for water on a 2.5-m carbowax 1500 column. The differences between the blanks and the irradiated samples were used to calculate the G of water.

The acetaldehyde yield was determined polarographically (7).

The amount of formaldehyde was measured by the chromotropic acid method. Analyses were done in triplicate and three standard samples and a blank were done concurrently with the unknowns. The procedure for an individual analysis was as follows. Chromotropic acid (110 ± 1 mg) was weighed into each of seven 10-ml Erlenmeyer flasks and 0.80 ml of distilled water was added to each. Only a small portion of the chromotropic acid dissolved. Then 0.20 ml of irradiated ethanol, or of pure ethanol or standard ethanolic solution of formaldehyde, was added to the various flasks. Three different standard concentrations of formaldehyde were used to bracket the concentration in the unknowns. The solutions were then evaporated to dryness by suspending the flasks for 25 minutes in an oil bath at $110 \pm 2^{\circ}\text{C}$. The oil was stirred to obtain a uniform temperature for all the flasks in the bath. The flasks were then removed from the bath and allowed to cool for 3 or 4 minutes. Five milliliters of concentrated sulphuric acid was pipetted into each flask and they were then heated for 30 minutes in an oil bath at $130 \pm 2^{\circ}\text{C}$. After the flasks were removed from the bath and cooled, the acid solutions were transferred into 50-ml, glass-stoppered flasks. The solutions were diluted with 15.0 ml of distilled water, cooled, and their optical densities measured at 570 $\text{m}\mu$. The temperatures and times in the analytical procedure should be kept as constant as possible and the diluted solution should not stand more than 1 hour before being measured in a spectrophotometer (the color fades). The sensitivity of the method decreases markedly if the water/ethanol ratio in the initial chromotropic acid solution decreases below 4/1. Acetaldehyde does not interfere with the analysis.

RESULTS

Pure ethanol was subjected to alpha radiation and the gaseous-product yield distribution was studied as a function of dose over the range 0.50×10^{19} ev to 3.77×10^{19} ev. The total yield of gases noncondensable at -196°C , $G(-196)$, appears to be constant at 10.1 ± 0.4 over this dose range, while that of gases volatile at -112°C , $G(-112)$, decreases with increasing dose.

The products that constituted the fractions volatile at -196°C and -112°C were measured and their G values are presented as a function of dose in Fig. 1.

The yields of methane are the combined yields obtained from the two gas fractions. The portion of the total methane, derived from the -112°C fraction, increased from 21% at the lowest dose to 58% at the highest dose. However, the methane yield obtained from the gases volatile at -196°C remained approximately constant with a G of 1.1 ± 0.1 except for the lowest-dose experiment.

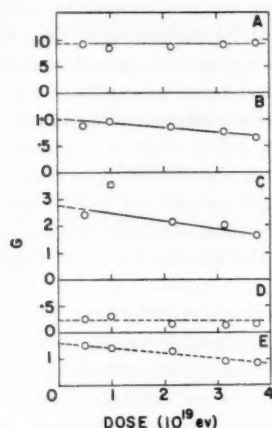


FIG. 1. G values of products volatile at -196°C and -112°C , as a function of dose: (A) hydrogen, (B) carbon monoxide, (C) methane, (D) ethane, (E) ethylene. The sample was 1.6 ml liquid ethanol volatilized into a 1-l. bulb at 108°C .

Since the amounts of liquid products were too small to be measured in these dose-function experiments, appreciably higher doses, about 8×10^{20} ev, were given to three ethanol samples and the liquid products were measured. The average yields are given in Table I along with the yields of the gaseous products obtained at the same dose. Comparison of the gaseous product yields in Table I and Fig. 1 indicates little change in the

TABLE I
 G values of products obtained by irradiating ethanol vapor
(Irradiation temperature 108°C , dose $\approx 8 \times 10^{20}$ ev)

Product	G	Product	G
Hydrogen	7.6	Formaldehyde	0.9
Carbon monoxide	1.1	Acetaldehyde	4.5
Methane	1.66	Propanol	0.6
Ethane	0.23	Butanol	0.19
Ethylene	0.72	1,2-Propanediol	0.15
Acetylene	0.03	2,3-Butanediol	1.2
C ₃ and C ₄ hydrocarbons	Trace	Total glycols	1.6
Water	5.4		

dose region from about 4 to 80×10^{19} ev.

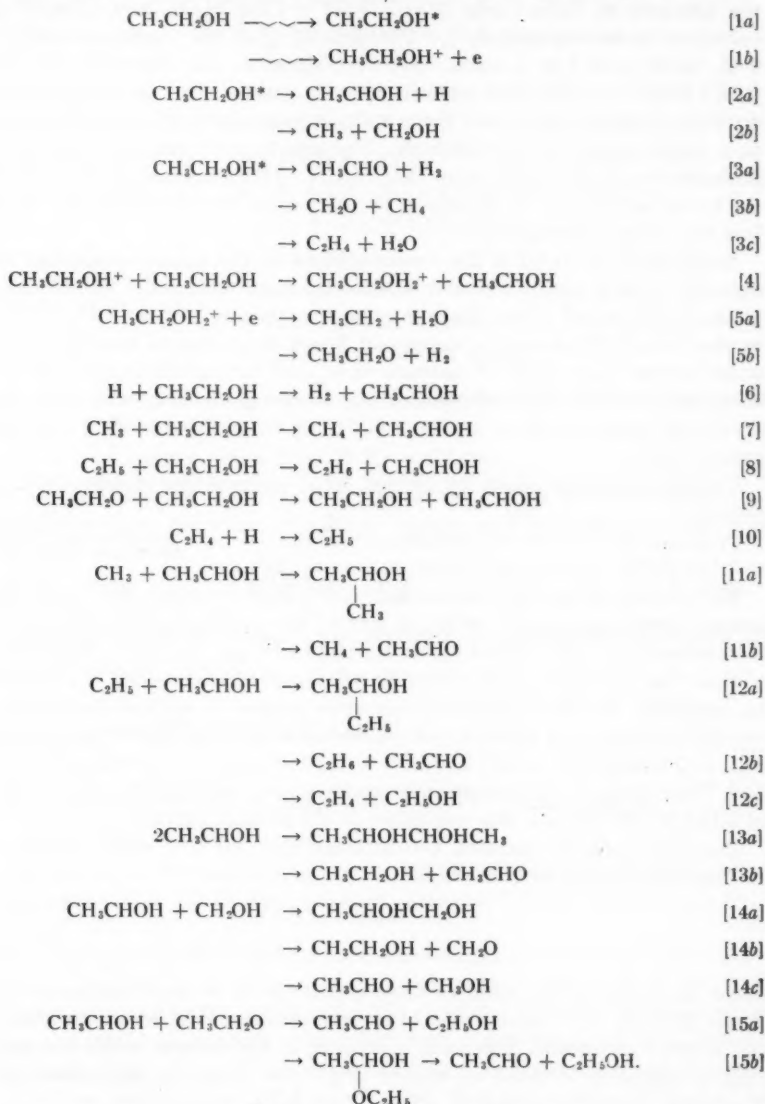
There is fair agreement between the total glycols (ucon column) and the sum of the vicinal glycols (carbowax column). Ethylene glycol, 1,3-butanediol, and 1,4-butanediol were not present in detectable amounts.

DISCUSSION

The values of $G(\text{H}_2)$ obtained in the previous investigations of liquid ethanol (1-3) are around 4. The present vapor phase radiolysis of ethanol has yielded an average value of $G(\text{H}_2) = 8.9 \pm 0.4$ in the dose region from 0.5 to 3×10^{19} ev/g. In hydrocarbon

radiolyses, the 100-ev hydrogen yields are also larger in the gas phase reactions than in the liquid phase reactions (5).

The following mechanism is suggested to account for the observed reaction products:



Reactions [4] and [5a, b] are quite speculative but they are being considered in an investigation of the radiolysis of liquid ethanol in this laboratory. It is assumed that the positive charge on the species in reactions [4] and [5a, b] is localized on the oxygen atom.

Acetaldehyde may be formed by reactions [3a], [11b], [12b], [13b], [14c], and [15a, b]. The radicals involved in these reactions are CH_3 , C_2H_5 , $\text{CH}_3\text{CH}_2\text{O}$, CH_3CHOH , and CH_2OH . From the G values of products which require these radicals for their formation, the amounts of CH_3 , C_2H_5 , $(\text{CH}_3\text{CHOH} + \text{CH}_3\text{CH}_2\text{O})$, and CH_2OH radicals can be calculated to be respectively 1.1–2.3 (depending on the mechanism of formation of CO), 0.43, 12.35, and 1.05 G units. Since the amount, and therefore the concentration, of $(\text{CH}_3\text{CHOH} + \text{CH}_3\text{CH}_2\text{O})$ radicals is much greater than that of any other radical, the disproportionation reaction of these radicals (reactions [13b] and [15]) might be considered as a major source of acetaldehyde. The steady-state concentration of $\text{CH}_3\text{CH}_2\text{O}$ will probably be much smaller than that of CH_3CHOH because of reaction [9] and because the latter radicals can be generated in many more reactions than can the former radicals (see the above mechanism).

Since the C—C bond is the weakest bond in the ethanol molecule, one might have expected a large yield of products resulting from CH_3 and CH_2OH radicals in the gas phase. In the liquid phase, there may be recombination of the CH_3 and CH_2OH radicals in the Franck-Rabinowitch cages and hence the yields of the corresponding products would be low. Low yields of methane (0.43) and formaldehyde (0.3) were experimentally observed by McDonnell and Newton (1). In the gas phase, where the cage effect is not operative, larger yields of methane (1.7) and formaldehyde (0.9) were observed in the present work.

Carbon monoxide might be formed by decomposition of formaldehyde and acetaldehyde.

Propanol and butanol are probably formed by the addition of methyl and ethyl radicals to CH_3CHOH radicals (reactions [11a] and [12a]).

The vicinal glycols (2,3-butanediol and 1,2-propanediol) that were measured in the present investigation were probably formed by combination of CH_3CHOH radicals with themselves and with CH_2OH radicals (reactions [13a] and [14a]). From the relative yields of these two glycols it may readily be calculated that the yield of ethylene glycol would be negligible. If $\text{CH}_3\text{CH}_2\text{OH}$ radicals were present in appreciable concentration during the decomposition of ethanol, the combination of $\text{CH}_3\text{CH}_2\text{OH}$ radicals with each other and with CH_3CHOH would have led to the formation of 1,4-butanediol and 1,3-butanediol. Since these products were not produced to a measurable extent, the concentration of $\text{CH}_3\text{CH}_2\text{OH}$ radicals was negligible in the present system.

The ethyl radicals produced by reactions [5a] and [10] might abstract (reaction [8]) or disproportionate to give ethane.

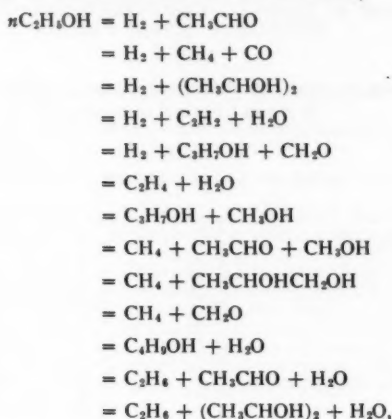


Since the value of the ratio of disproportionation to combination of ethyl radicals is about 0.12 (9), the amount of ethane from reaction [16b] would be about one-eighth of the amount of butane. The yield of butane in the present work was only a trace, and thus a negligible amount of ethane originates from the disproportionation reaction. Therefore the major source of ethane is probably reaction [8].

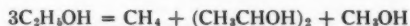
Ethylene, which has an appreciable yield, is assumed to be formed by reactions [3c], [12c], and [16b]. Since [16b] was precluded as a significant source of ethane, it may also be neglected as a source of ethylene.

It is not known whether the acetylene is a primary or a secondary product but it will be assumed to be mechanistically as well as stoichiometrically equivalent to $(\text{C}_2\text{H}_4 - \text{H}_2)$.

The preceding mechanism can be reduced to the following stoichiometric equations:



where $n = 1, 2$, or 3 . The products can be written in several equivalent combinations. Equations such as



can be included without altering the over-all picture or the calculations that follow.

From the above equations, the yields of hydrogen, water, and methane were correlated to the yields of other products.

$$G(\text{H}_2) = G(\text{CH}_3\text{CHO} + \text{CO} + (\text{CH}_3\text{CHOH})_2 + \text{C}_2\text{H}_2 + \text{C}_3\text{H}_7\text{OH} - \text{CH}_3\text{OH} - \text{C}_2\text{H}_6)$$

Using Table I, the sum of the G values of the products on the right-hand side of this equation is equal to $7.2 - G(\text{CH}_3\text{OH})$.

Similarly

$$\begin{aligned}
 G(\text{H}_2\text{O}) &= G(\text{C}_2\text{H}_2 + \text{C}_2\text{H}_4 + \text{C}_4\text{H}_9\text{OH} + \text{C}_2\text{H}_6) \\
 &= 1.2,
 \end{aligned}$$

$$\begin{aligned}
 G(\text{CH}_4) &= G(\text{CO} + \text{CH}_3\text{OH} + \text{CH}_3\text{CHOHCH}_2\text{OH} + \text{CH}_2\text{O} - \text{C}_3\text{H}_7\text{OH}) \\
 &= 1.55 + G(\text{CH}_3\text{OH}).
 \end{aligned}$$

The values of $G(\text{H}_2) = 7.2 - G(\text{CH}_3\text{OH})$ and $G(\text{CH}_4) = 1.55 + G(\text{CH}_3\text{OH})$ are in approximate agreement with the observed values, $G(\text{H}_2) = 7.6$ and $G(\text{CH}_4) = 1.66$, if $G(\text{CH}_3\text{OH})$ is small.

From the above, an approximate expected yield of methanol would be $G(\text{CH}_4) - 1.55 \approx 0.1$. In the liquid phase radiolysis of ethanol (1), the value of the ratio of the yields of formaldehyde to methanol is 0.2. If this ratio had the same value in the vapor phase, the expected yield of methanol would be about 0.2. Thus the methanol yield is probably quite small, although methanol could not be measured by the present analytical system.

The predicted value of $G(\text{H}_2\text{O}) = 1.2$ is much lower than the observed value of 5.4. The source of this excess water is not obvious. It might have been formed by reactions not considered in the mechanism, or the sample might have absorbed water from the atmosphere during the analytical procedure. However, the analysis of the blank samples should have compensated for the latter possibility. An unaccountable excess of water was also observed by McDonell and Newton (1) in the liquid phase radiolysis of ethanol.

A mass balance for carbon, hydrogen, and oxygen has been worked out from the products and is presented in Table II. This mass balance corresponds to an empirical

TABLE II
Mass balance of carbon, hydrogen, and oxygen in the products obtained
in the radiolysis of ethanol vapor

Product	G	Mass balance		
		C	H	O
Hydrogen	7.6	—	15.2	—
Carbon monoxide	1.1	1.1	—	1.1
Methane	1.66	1.7	6.6	—
Ethylene	0.72	1.4	2.9	—
Ethane	0.23	0.5	1.4	—
Acetylene	0.03	0.1	0.1	—
Water	5.4	—	10.8	5.4
Formaldehyde	0.9	0.9	1.8	0.9
Acetaldehyde	4.5	9.0	18.0	4.5
Propanol	0.6	1.8	4.8	0.6
Butanol	0.19	0.8	1.9	0.2
1,2-Propanediol	0.15	0.5	1.2	0.3
2,3-Butanediol	1.2	4.8	12.0	2.4
Total		22.2	76.7	15.4

NOTE: The numbers under C, H, and O in the table were obtained by multiplying the G value of the product by the respective number of atoms of C, H, or O in that product.

formula $C_{2.00}H_{6.76}O_{1.36}$, which has slightly more hydrogen and oxygen in it than does ethanol, C_2H_6O .

If water is generated only by reactions [3c] and [5a], then $G(H_2O)$ should be equal to 1.2. The excess water in G units is $(5.4 - 1.2) = 4.2$. If the corresponding amounts of H (8.4) and O (4.2) are subtracted from the mass balance in Table II, the empirical formula of the total products becomes $C_{2.00}H_{6.02}O_{0.99}$.

This good mass balance indicates that little or no polymer was formed during irradiation, unless polymer was a coproduct of the observed excess of water. It was also observed that the Po^{210} -alpha-particle source intensity showed no decrease during the ethanol irradiations. In the radiolysis of hydrocarbons (5, 8), there was a poor mass balance and a decrease in source intensity due to the deposition of polymer on the surface of the source. The lack of decrease in source intensity and a good mass balance in the ethanol products corroborate little or no polymer formation during the radiolysis of ethanol.

It might be mentioned that the decrease in the yields of CO , CH_4 , and C_2H_4 between 0.5 and 4×10^{19} ev does not appear to be accompanied by a comparable decrease in the hydrogen yield (Fig. 1). Thus the decrease does not appear to be entirely a scavenging effect.

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THE RADIOLYSIS OF ETHANOL

II. BINARY VAPOR MIXTURES¹

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ABSTRACT

Benzene and cyclohexene cause a marked decrease in the hydrogen yield from the vapor phase radiolysis of ethanol.

The experimental data were tested against the two reaction mechanisms that gave straight-line plots for the corresponding cyclohexane-protector systems. Both of these mechanisms also gave straight-line plots for the ethanol-protector systems.

One mechanism involved scavenging of hydrogen atoms. The values of the kinetic parameters derived from this mechanism are quite similar in the cyclohexane and ethanol systems.

The second mechanism involved the transfer of energy (excitation or ionization) from ethanol to the protector. The values of the kinetic parameters derived from this mechanism showed some differences between the ethanol and cyclohexane systems.

One possible reason for the lack of resolution between the two reaction mechanisms might be that they both occur to comparable extents. Two mechanisms appear to occur to comparable extents in the liquid cyclohexane system.

INTRODUCTION

In the isolation of steps in radiolytic mechanisms, the study of binary systems should be very helpful. In that connection, the radiolyses of mixtures of hydrocarbons have been frequently investigated (1-5). However, the radiolyses of organic compounds with functional groups and of their mixtures with other compounds are less common. As a part of a general program, we have investigated the vapor phase radiolysis of ethanol by Po^{210} alpha particles (6). Newton and McDonell (7) were the first to report the protection of liquid ethanol by acetaldehyde and by hexene. The present paper reports the results of a study of the protective effect of benzene and of cyclohexene on ethanol during radiolysis in the vapor phase.

EXPERIMENTAL

The ethanol used in these investigations was obtained from Reliance Chemical Ltd. and contained about 0.11 mole% water. The benzene was Eastman Kodak spectrograde and cyclohexene was from Matheson, Coleman and Bell. All the compounds were used without any further purification.

The apparatus used was a conventional vacuum manifold and the general techniques used in this investigation have been previously described (8, 9).

Binary vapor mixtures of ethanol and benzene or cyclohexene were irradiated at 108° C with Po^{210} alpha particles. The Po^{210} source (nominally 100 mc) was calibrated by Fricke dosimetry, using $G(\text{Fe}^{+++}) = 5.5$. The concentration of the protector in the vapor mixtures ranged from 2 to 100 mole% in each case. A quantity (1.6 ml) of well-degassed liquid solution was volatilized into a heated 1-liter reaction vessel that contained the Po^{210} source. The irradiation time was 2 hours. Approximately 0.01% of the sample was decomposed.

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RESULTS

The radiolysis of pure ethanol vapor has been studied as a function of dose (6). The major single product was hydrogen, with smaller amounts of carbon monoxide, methane, ethane, ethylene, acetaldehyde, formaldehyde, vicinal glycols, and water. Under the conditions of the present work, only the total fraction volatile at -196°C (comprised of about 80% H_2 , 10% CO , and 10% CH_4) could be measured accurately as a function of protector concentration.

The results are presented in Fig. 1. In these plots, the observed values of $G(-196)$,

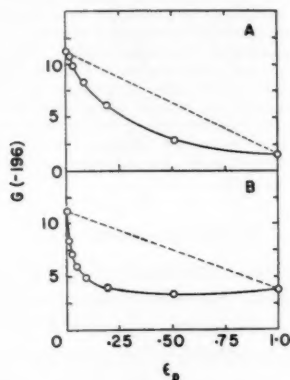


FIG. 1. $G(-196)$, gas fraction volatile at -196°C , as a function of protector concentration: ϵ_p = electron fraction of protector P; (A) P = benzene; (B) P = cyclohexene.

the 100-ev yield of the gas fraction volatile at -196°C , are plotted against the "electron fraction" of the protector, ϵ_p . The value of $G(-196)$ decreases with increasing inhibitor concentration in both the systems. It is clear from Fig. 1 that cyclohexene reduces the yield of the -196°C fraction more rapidly than does benzene. The broken lines in the plots indicate the yield that might have been expected if there had been no interaction between the components and if the energy absorption were directly proportioned to the electron fraction of the compounds.

DISCUSSION

The experimental data were tested against the two reaction mechanisms that gave straight-line plots for the binary vapor mixtures of cyclohexane and benzene, cyclohexene, or propylene (9). The two mechanisms will be treated separately, making the simplifying assumption that the variation of the total gas fraction volatile at -196°C is a measure of the variation of the hydrogen yield.

I. Scavenging Mechanism



In the above, I represents the rate of formation of $C_2H_5OH^*$, P represents the protector, and PH and $P\cdot$ represent the corresponding radicals. The following equation can be derived by steady-state treatment of the above mechanism:

$$\left\{ 1 + w \frac{(P)}{(C_2H_5OH)} \right\} \frac{I}{d(H_2)/dt} = 1 + v \frac{(P)}{(C_2H_5OH)} = \rho,$$

where $w = k_6/k_3$, $v = (k_4 + k_5)/k_3$, and ρ represents the left-hand side of the equation.

The numerical values of $I/[d(H_2)/dt]$ were determined from the experimental data (4).

By giving arbitrary values to w , sets of values of ρ were calculated. These sets of values were plotted against the ratio $(P)/(C_2H_5OH)$ to see whether a straight line with an intercept of unity could be obtained for each of benzene and cyclohexene. Such a line was obtained in each case (see Fig. 2). The values of the various ratios of rate con-

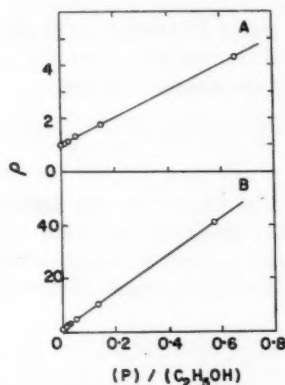


FIG. 2. Kinetic plots of mechanism I: $\rho = \{1 + w[(P)/(C_2H_5OH)]\} I/[d(H_2)/dt]$; (A) P = benzene; (B) P = cyclohexene.

stants derived from these plots are shown in Table I. The corresponding values obtained in the cyclohexane systems (9) are given in parentheses.

TABLE I
Values of rate-constant ratios obtained from mechanism I

P	k_2/k_3	k_4/k_3	k_5/k_3
C_6H_6	0.9 ± 0.3 (2.5 ± 0.2) ^a	4.2 ± 0.5 (5.9 ± 0.5)	4.7 (2.4)
C_6H_{10}	20 ± 5 (25 ± 10)	50 ± 10 (31 ± 19)	2.5 (1.2)

^aCorresponding cyclohexane system values given in parentheses.

It is apparent that the values obtained for the rate-constant ratios are rather similar in the cyclohexane and ethanol systems. While this similarity between the reactivities of ethanol and cyclohexane is not surprising (the rates of reaction of methyl radicals with cyclohexane and ethanol are approximately equal at 182° C and their activation energies are similar (10)), the same comments that were made in the earlier paper (9) can be

repeated here. The values of the rate-constant ratios obtained with cyclohexene might not be unreasonable. However, the value of k_6/k_3 obtained from benzene is surprisingly high, even if the hydrogen atoms are epithermal. It implies that abstraction of hydrogen atoms from benzene is as easy as from ethanol. The much stronger C—H bonds in benzene than in ethanol make this seem unlikely.

Now consider the second mechanism.

II. Energy (Ionization or Excitation) Transfer Mechanism



The x signifies that perhaps not every P^* results in the formation of a hydrogen molecule. Reactions [6] and [8] represent over-all processes and might comprise several steps each. Steady-state treatment of this mechanism yields

$$\{1 + y(\text{P})\} I' / d(\text{H}_2) / dt = 1 + z(\text{P}) = \rho'$$

where $y = xk_7/k_6$, $z = k_7/k_6$, and ρ' represents the left-hand side of the equation. Assuming arbitrary values for y , sets of values of ρ' were calculated and plotted against the protector concentration (P), in an attempt to obtain a straight line with an intercept of unity. Figure 3 shows the lines that were obtained. The value of y that gave the desired

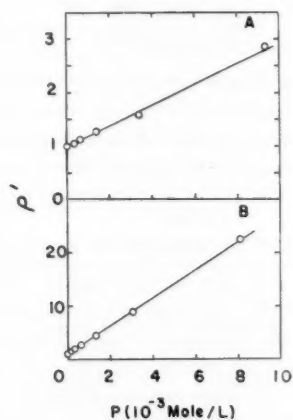


FIG. 3. Kinetic plots of mechanism II: $\rho' = \{1 + y(\text{P})\} I' / d(\text{H}_2) / dt$; (A) P = benzene; (B) P = cyclohexene.

line in each system, along with the slope of the line, z , and the corresponding value of x , are presented in Table II. The values obtained in the corresponding cyclohexane systems (9) are given in parentheses.

TABLE II
Values of kinetic parameters obtained from mechanism II

<i>P</i>	<i>y</i> (liter/mole)	<i>x</i>	<i>z</i> (<i>k</i> ₇ / <i>k</i> ₈ (liter/mole))
C ₆ H ₆	6±6 (150±18) ^a	0.03±0.03 (0.25±0.01)	190±20 (610±25)
C ₆ H ₁₀	720±180 (1200±420)	0.28±0.01 (0.46±0.01)	2600±600 (2700±800)

^aCorresponding cyclohexane system values given in parentheses.

Table II shows certain differences between the cyclohexane and ethanol systems. The apparent value of *x* (the fraction of the P*, activated by energy transfer from the substrate, that decomposes to yield H₂) is smaller in the ethanol systems than in the cyclohexane systems. Also, the apparent value of the ratio *k*₇/*k*₈ (the ratio of the rate of energy transfer to the rate of decomposition of the activated substrate species) is smaller in ethanol-benzene than in cyclohexane-benzene, while it is the same in the two systems containing cyclohexene.

It does not seem useful to speculate here upon the possible reasons for these similarities and differences. Further work, especially using compounds with widely differing ionization potentials and hydrogen-atom activities, is required.

It may be remarked, however, that one possible reason for the present lack of resolution between the scavenging and energy-transfer mechanisms might be that they both occur to comparable extents. Two mechanisms appear to occur to comparable extents in the liquid cyclohexane systems (4). It is possible that the rate constants and concentrations are such in the gas phase that the two mechanisms will be difficult to resolve.

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NOTES

β,β,β -TRIFLUOROLACTIC ACID¹

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In a search for inhibitors of lactic acid dehydrogenase it was of interest to prepare and evaluate the hitherto unknown β,β,β -trifluorolactic acid. Our synthesis was effected by a straightforward route patterned after the preparation of α -methyl- β,β,β -trifluorolactic acid (1). Trifluoroacetaldehyde (2) was treated with hydrogen cyanide and the intermediate cyanohydrin was hydrolyzed by vigorous treatment with sulphuric acid to yield the desired *dl*-acid as a crystalline solid.

Trifluorolactic acid and its sodium salt were not oxidized by a crystalline rabbit muscle lactic dehydrogenase in the presence of DPN nor did they inhibit the enzymatic oxidation of sodium lactate or the reduction of sodium pyruvate. The procedure used was similar to that described by Busch and Nair (3) and by Baker and co-workers (4).

EXPERIMENTAL

The infrared spectrum was determined with a Beckman model IR4 instrument, while ultraviolet determinations were made with a Carey model 14 recording spectrophotometer.

β,β,β -Trifluorolactic Acid

Cold 16 *N* sulphuric acid (108 ml) was added dropwise over a period of 1 hour to a solution of trifluoroacetaldehyde hydrate (2) (39.2 g), potassium cyanide (21.6 g), and water (83 ml), held at 0–5°. The mixture was then allowed to come to room temperature and stand for 16 hours. Extraction with ether (4×125 ml), removal of solvent after sodium sulphate drying, and distillation of the residue at reduced pressure gave 33.3 g of intermediate cyanohydrin,² b.p. 75–76° (45 mm). The cyanohydrin (30 g) was added dropwise over a 10-minute period to concentrated sulphuric acid (29 ml) with a considerable evolution of heat ensuing as well as the appearance of a thick precipitate. The temperature was slowly raised to 120° and held there for 15 minutes before the mixture was cooled and cautiously diluted with ice water (150 ml). The resulting solution was boiled for 10 hours under reflux and then cooled, saturated at room temperature with sodium sulphate, and extracted with ether (4×125 ml). The ether extract was washed once with saturated sodium sulphate and then dried, and the solvent removed at atmospheric pressure. The residue was distilled at 60–95° (1–2 mm) through a short-path condenser and yielded 23.6 g of β,β,β -trifluorolactic acid as a solid, m.p. 64–67°. An analytical specimen was obtained by recrystallization from methylene chloride – pentane, m.p. 68–69°. Infrared: $\lambda_{\text{max}}^{\text{KBr}}$ 5.69 μ . Anal. Calc. for $\text{C}_3\text{H}_3\text{F}_3\text{O}_3$: C, 25.01; H, 2.10; F, 39.57. Found: C, 25.42; H, 2.28; F, 39.35.

Attempted Enzymatic Oxidation of Trifluorolactic Acid and Inhibition Studies

The following solutions were added successively to a cuvette: 0.1 *M* phosphate buffer, pH 8.5 (2.7 ml), lactic dehydrogenase³ (5 γ in 0.1 ml of buffer), DPN (1.2 mg in 0.1 ml

¹This work was aided by grant No. T-185 from the American Cancer Society.

²A sample of cyanohydrin allowed to stand for 1 week at room temperature polymerized.

³Purchased from Worthington Biochemical Corporation.

of water), and trifluorolactic acid or sodium trifluorolactate (1–40 mg in 0.1 ml phosphate buffer). Readings were taken at 15-second intervals in the spectrophotometer at 340 $m\mu$ to follow the appearance of DPNH but no oxidation of substrate occurred over a 30-minute period. When sodium *dl*-lactate (2.2 mg in 0.1 ml of phosphate buffer) was substituted for trifluorolactate, DPNH appeared at an initial rate of 0.05 optical density units per 15 seconds and the addition of varying amounts of trifluorolactate (1–40 mg) did not influence the rate of oxidation.

The reduction of pyruvate to lactate was carried out by the addition to a cuvette of 0.1 *M* phosphate buffer, pH 7.4 (2.7 ml), lactic dehydrogenase (5 γ in 0.1 ml of buffer), DPNH (0.3 mg in 0.1 ml of water), and sodium pyruvate (0.55 mg in 0.1 ml of buffer). Readings at 340 $m\mu$ showed an initial decrease of 0.2 optical density units per 15 seconds. The addition of up to 10 mg of sodium trifluorolactate in buffer solution, previous to the addition of sodium pyruvate, did not inhibit the reduction of pyruvate.

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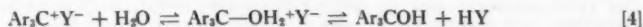
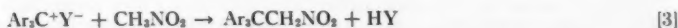
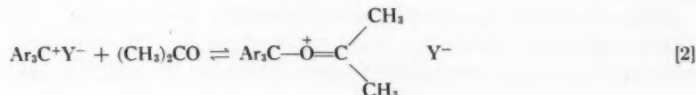
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CARBONIUM PERCHLORATES IN CHLOROFORM SOLUTION

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In connection with other work on the spectra of carbonium ions, we have examined the behavior of triarylmethyl perchlorates in chloroform solution. The lowering in the apparent degree of ionization (1–12) of triarylmethyl salts dissolved in organic solvents has been the subject of some speculation. Several reactions might occur, including: (a) repression of the ionization of carbonium salts in the organic medium (1) (eq. [1]); (b) co-ordination of the carbonium ion with a solvent molecule, for example ether (4, 12) or acetone (7) (eq. [2]); and (c) solvolysis reactions (10) which would include both the reaction of the carbonium ion with an organic solvent molecule, for example nitromethane (9) (eq. [3]), and hydrolysis to the carbinol by traces of water remaining in the imperfectly dried solvents (11) (eq. [4]).



We have examined chloroform as a solvent since it is unlikely to co-ordinate with carbonium ions. Unlike carbon tetrachloride, however, it will dissolve reasonable amounts of carbonium salts.

EXPERIMENTAL

Solvents

Reagent grade chloroform was washed with 95% sulphuric acid followed by repeated washings with distilled water and was then dried over CaCl_2 and P_2O_5 . Distillation under nitrogen from Drierite through a 30-cm fractionating column yielded a fraction which was stored in a dark bottle under nitrogen over anhydrous potassium carbonate. The bottle was equipped with a drying tube and a siphoning arrangement. Partially dried solvents were prepared in the same manner but were dried for shorter periods. "Wet" chloroform was prepared by saturating this material with water at 10° . Its water content was estimated from solubility data to be $3.5 \times 10^{-2} M$.

Reagents

Triphenylmethyl perchlorate and tris-*p*-methoxyphenylmethyl perchlorate were prepared essentially as described by Hofmann and Kirmreuther (13). Tri-*p*-tolylmethyl perchlorate was prepared by the addition of perchloric acid and dry ether to an acetic anhydride solution of the carbinol. The product was recrystallized from acetic anhydride-ether and freed from solvent under vacuum. Titration with standard potassium hydroxide gave a molecular weight of 389; calculated, 384. Tri-*p*-tolylcarbinol was prepared by the Grignard reaction of *p*-tolylmagnesium bromide on di-*p*-tolyl ketone. The crude product was purified through the chloride which was then hydrolyzed by sulphuric acid to the carbinol. Recrystallization from petroleum ether gave the product, m.p. $94-96^\circ$.

Measurements

A sample of the perchlorate (5-15 mg) was weighed into a dry volumetric flask and dissolved in acetic anhydride. Aliquots (0.05-0.5 ml) of this solution were transferred to 5-ml volumetric flasks and evaporated to dryness under vacuum. Dry air was then admitted to the flask. The succeeding operations of filling the flask with solvent and then filling the glass-stoppered absorption cells with solvent were carried out in a dry box. Light absorption measurements were made on a Beckman DU or a Cary, Model 14 spectrophotometer. Since the color intensities in the chloroform were temperature dependent (except for the *p*-methoxy compound) the cell compartment was kept at $25.0 \pm 0.2^\circ$. Optical densities of more-concentrated solutions were measured using 0.1-cm cells. A very rapid initial partial fading, which could not be followed, occurred with the tri-*p*-tolyl and triphenyl compounds. This was followed by a slow fading reaction which obeyed exact second-order kinetics. This was corrected for by extrapolation to zero time.

RESULTS

The absorption spectra of the triarylmethyl perchlorates in chloroform in the visible region were very similar to those obtained in 50-70% sulphuric acid* except that the absorption maxima were shifted from 2-8 μ to the red. The quantity $D_{\lambda_{\text{max}}} / \int D d\lambda$, the

*We have observed that the carbonium ion spectrum for each of these compounds is altered in more-concentrated sulphuric acid. These changes, which are still being investigated, become marked in regions above 80%, 100%, and 102% sulphuric acid for tris-*p*-methoxyphenylmethyl, tri-*p*-tolylmethyl, and triphenylmethyl cations, respectively, and may account for some of the discrepancies in carbonium ion spectra reported in the literature.

optical density at the wavelength maxima divided by the area under the curve, was identical to within 2% in sulphuric acid and chloroform.

The variation of optical density with concentration of dissolved salt is shown in Fig. 1

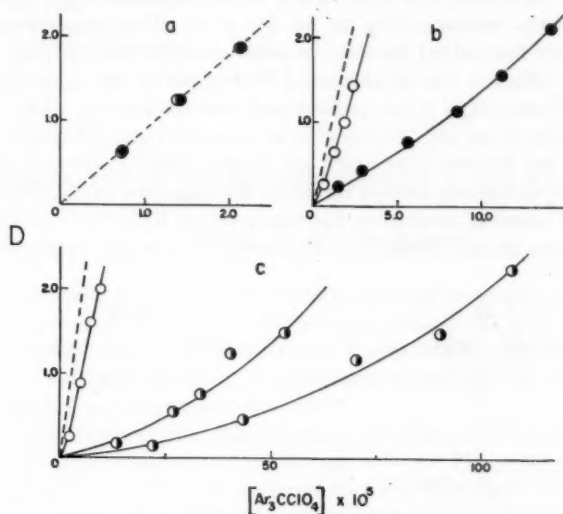


FIG. 1. Variation of optical density with molarity of dissolved triarylmethyl perchlorate. (a) $(p\text{-CH}_3\text{OC}_6\text{H}_4)_3\text{C}^+\text{ClO}_4^-$, (b) $(p\text{-CH}_3\text{C}_6\text{H}_4)_3\text{C}^+\text{ClO}_4^-$, (c) $(\text{C}_6\text{H}_5)_3\text{C}^+\text{ClO}_4^-$; \circ dry CHCl_3 , \bullet partially dried CHCl_3 , \bullet wet CHCl_3 ; the broken line corresponds to the extinction coefficient found for the carbonium ions in H_2SO_4 (Table I).

TABLE I
Spectral data for carbonium perchlorates

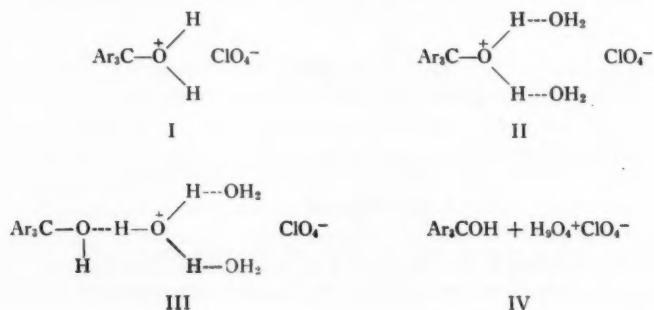
Tris- <i>p</i> -methoxyphenol			Tri- <i>p</i> -tolyl			Triphenyl		
Solvent	λ_{max} (m μ)	$\epsilon \times 10^{-4}$	Solvent	λ_{max} (m μ)	$\epsilon \times 10^{-4}$	Solvent	λ_{max} (m μ)	$\epsilon \times 10^{-4}$
56.8% H_2SO_4	484	8.8	83.0% H_2SO_4	452	9.0	96.0% H_2SO_4	433	3.8
CHCl_3	492		CHCl_3	454		CHCl_3	435	

for the three carbonium perchlorates dissolved in both "dry" and "wet" chloroform. It can be seen that the ionization of tris-*p*-methoxyphenylmethyl perchlorate is complete in both wet and dry chloroform and that hydrolysis of this highly resonance stabilized carbonium ion does not proceed to a measurable extent. (The excellent agreement in Fig. 1a between the experimental points for chloroform solution and the line for 56.8% sulphuric acid may be fortuitous since a somewhat *higher* extinction coefficient has been reported for this ion in nitrobenzene (3).)

Tri-*p*-tolylmethyl perchlorate and triphenylmethyl perchlorate both show a reduction in the concentration of carbonium ion, particularly the triphenyl compound in the partially dried solvent (Fig. 1c). A wet chloroform solution of the latter could not be studied since a turbid solution resulted when sufficient perchlorate was used to produce a measurable color. The difficulty in obtaining reproducibly "dry" samples of chloroform precludes any exact comparison between the three perchlorates in the dried and partially dried solvents.

Since all the triarylmethyl perchlorates are highly colored in the solid state, it is generally believed that covalent forms of these compounds are unimportant. The approach, in the present cases, to complete ionization, which accompanies rigorous drying of the solvent is in accord with this. The slow fading of the carbonium ion color may be due to a solvolysis reaction corresponding to eq. [3] or to ether formation, but it seems unlikely that the very fast initial decrease in color could be due to this. We believe, in fact, that the latter effect is due to the rapid hydrolysis of the carbonium perchlorate ion pair by the small amount of water present and that the curves in Fig. 1 are explained by the equilibria shown in eq. [4]. (Traces of acid present in the chloroform would reverse these reactions but we believe that acids are absent since prolonged treatment with anhydrous potassium carbonate always *increased* the apparent extinction coefficient.)

There are several possible structures for the colorless hydrolysis product, and their relative concentrations should depend on the amount of water present.



Specific solvation effects such as those shown above involving hydrogen bonding (14, 15) will be most important in the low dielectric solvent chloroform. With a limited amount of water it seems likely that I would be formed whereas in the wetter solutions the carbinol would be expected to become less and less important in the dispersal of the positive charge. That is, the ion pairs II, III, and eventually IV, the carbinol plus the normal hydrated form of perchloric acid (16, 17), should become the principal cations in solution.

ACKNOWLEDGMENT

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THE POLARIZATION OF THE FLUORESCENCE OF 1- AND 2-NAPHTHOIC ACID¹

ROBIN M. HOCHSTRASSER

The naphthoic acids have received considerable spectroscopic attention within recent years. Weller (1) and, more recently, Porter and Jackson (2) have determined pK values for the lowest excited states of the molecule. Kasha and El Bayoumi (3) have measured solvent spectral shifts in solution. Hochstrasser examined the fluorescence and phosphorescence spectra in various solvents (10).

Porter and Jackson concluded that excitation to the lowest excited singlet level of the acids involves an orbital promotion of the type $n \rightarrow \pi^*$. This conclusion was based on the vastly different pK values for the molecule in its ground and first excited singlet state. The large difference in pK ($pK^* - pK = 8$ units) quoted by these authors applies to the protonated acid-acid equilibrium and not, as stated, to the acid-anion equilibrium (1). The value of ΔpK for the anionic system is about 2-4 units (5). Therefore the conclusions regarding the orbital nature of the lowest excited singlet level are not convincing.

On the basis of absorption intensity and solvent effects, El Bayoumi and Kasha assumed that the first excited singlet state is of π, π^* character, for which only slight changes of acid strength would be predicted.

Absorption spectra need not always provide proof of the character of the *lowest excited level* of a molecule. If absorption to this state is very weak, as for example would be the case for an $n \rightarrow \pi^*$ transition, a nearby strong transition, e.g. $\pi \rightarrow \pi^*$, could mask the weak transition. This is especially true for organic acids since the absorption spectra are characteristically diffuse.

Fluorescence originates from the lowest excited singlet level for essentially all common polyatomic molecules. Thus only by means of emission studies of diffuse spectra can conclusive data be obtained for extremely weak bands which lie very close to stronger bands. In this note some results on the polarized emission spectra of thin crystals of 1- and 2-naphthoic acid are presented in order to determine the direction of the transition moment connecting the ground and emitting levels.

The crystal structures of 1-naphthoic acid (6) and of 2-naphthoic acid (7) are known and these provide the exact orientations of the molecules in the unit cell. For both acids the crystal is composed of planar dimeric units and for 1-naphthoic acid the normal to the dimer plane is nearly coincident with the crystallographic b -axis. Very thin ($\sim 30 \mu$), microscopically perfect plates were prepared by sublimation. The crystals were mounted on quartz disks with the b -axis vertical and the blue fluorescence (excited by Hg 3130 Å) was observed normal to the 100 face. The emission was analyzed by a polaroid sheet

¹This work was supported by a grant from the National Research Council of Canada.

and detected by our modified Hilger E2 spectrograph (4). The emitted intensities polarized parallel to the crystallographic axes were either maximal or minimal. The spectra was measured with the crystals at 300° K.

Crystallographic Data

The data of Trotter (6, 7) were used for the descriptions that follow. 'Oriented gas' intensity ratios were calculated from known atomic co-ordinates.

1-Naphthoic acid.—The crystal is monoclinic (space group $P2_1/a$) with $\beta = 92.2^\circ$. The unit-cell dimensions are $a = 31.12$, $b = 3.87$, $c = 6.92$ Å. The acid crystallizes, either from solution or after sublimation, in prisms which are elongated along the b -axis with (100) developed. The aromatic rings of the centrosymmetric dimer and the carboxyl (hydrogen-bonded) ring are not in the same plane. The deviation from coplanarity amounts to approximately 11° . The 'oriented gas' intensity ratio for a transition polarized perpendicular to the carboxyl plane is $I_b/I_c = 2.6$ while the value of this ratio for moments perpendicular to the aromatic ring planes is 4.2. The molecules are so arranged in the crystal that a line with any direction, but lying on the molecular plane (aromatic or carboxyl), always has a larger projection on the c than on the b crystallographic axis. This line need only deviate by a small angle from the plane for I_b/I_c to exceed unity. For example, the values of I_c/I_b (in parenthesis) for the lines joining certain carbon atoms of the 1-naphthyl group are as follows: 1,4 (4.5); 2,7 (6.9); 1,5 (1.4); 2,6 (6.3). Thus, for this crystal, a measurement of the dichroic ratio in absorption or the intensity ratio in emission normal to the (100) face should indicate unambiguously whether or not the electronic transition is polarized in or out of plane.

2-Naphthoic acid.—The crystal is monoclinic ($P2_1/a$) with $\beta = 92.6^\circ$; $a = 30.59$, $b = 5.00$, $c = 5.63$ Å. The acid crystallizes as prisms elongated along the b -axis and sublimation flakes are developed on (100). The aromatic and carboxyl planes are parallel within experimental limits. The intensity ratio normal to (100) cannot give nearly so much information in this case. Both in-plane and out-of-plane transitions may be b -polarized. Values of I_b/I_c are as follows: 1.43 (normal to the plane of the dimer); 4.0 (longest axis of naphthyl); 3.6 (shortest axis of naphthyl). If the measured value is greater than 1.43 yet less than 3.6 there is good indication that the transition moment lies in the molecular plane.

The Fluorescence of 1-Naphthoic Acid

The emission spectrum is a broad band with a peak intensity at 4415 Å. The intensity ratio I_c/I_b was 1.8:1. The polarization ratio is consistent with a transition moment in the molecular plane, directed along a line which joins the bisectors of 1—2 and 5—6 bonds of a naphthalene ring. However, this conclusion neglects crystal-induced mixing of oppositely polarized states which could considerably modify the presently assumed 'oriented gas' model.

The Fluorescence of 2-Naphthoic Acid

The fluorescence was broad and structureless with an intensity maximum at 4565 Å. The polarization ratio was $I_b/I_c = 1.7$, which suggests a transition moment in the plane of the molecule.

The Assignment of the Nature of the Transitions

$n \rightarrow \pi^*$ promotional transitions correspond to the promotion of an electron from the lone-pair orbital of the carbonyl oxygen (or the acidic oxygen) into an antibonding π -orbital which is mainly localized on the carbonyl group. Such transitions between

orbitals which are respectively symmetric and antisymmetric to reflection in the molecular plane are necessarily polarized perpendicular to the molecular plane. $\pi \rightarrow \pi^*$ transitions are polarized in the molecular plane. The allowed levels in the C_{2h} symmetry of the dimer are B_u (x - and y -polarized) and A_u (z or \perp polarization). Therefore the vibronic symmetry of the emitting level is B_u and the nature of the transition from this level to the ground state is $B_u \rightarrow A_g$ ($n^2\pi\pi^* \rightarrow n^2\pi^2$).

The excited states of the monomer are probably split by exciton interaction (8) in the dimer. If the monomeric lowest excited level is considered to lie in the plane and along the long axis of the aromatic ring, the resulting dimer states are A_g and B_u in order of increasing energy. Fluorescence from a dimer of this type would be an electronically forbidden transition. The order of dimer states is inverted for short-axis transition moments in the monomer. It is very likely that the lowest transition of the monomer involves contributions from both polarizations as in the case of unsubstituted naphthalene (9).

The transition-moment direction calculated from the observed polarization ratio for 1-naphthoic acid should correspond to the resultant of the monomeric moments. A theoretical computation (dipole-dipole approximation) of the dimer levels which arise from the interaction of two monomeric states of this nature yields the result that the lowest excited dimer level has B_u symmetry. This is consistent with the notion that the observed emission involves an allowed electronic transition $B_u \rightarrow A_g$ and is not mainly a vibronically allowed combination as would have to be the case if the lowest dimer excited state had the symmetry A_g .

Further results of the 1-naphthoic acid crystal are in preparation.

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IMPROVED PREPARATION OF BISTRIFLUOROMETHYLARSINE*

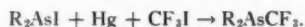
W. R. CULLEN

Bistrifluoromethylarsine was first prepared by reducing iodobistrifluoromethylarsine with either lithium aluminum hydride (16% yield) or zinc and hydrochloric acid (43% yield) (1). The reduction of chlorobistrifluoromethylarsine with lithium aluminum hydride has been reported to proceed smoothly at ca. -25° , giving a higher yield of bistrifluoromethylarsine (70%) (2). It has now been found that this method is unreliable

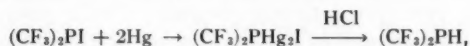
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and can result in complete failure. However, bistrifluoromethylarsine can be prepared by the reaction of chlorobistrifluoromethylarsine with excess hydrogen chloride, in the presence of mercury. The yield is high and the arsine can be easily separated from unreacted hydrogen chloride and the only other volatile reaction product, tetrakistrifluoromethyldiarsine.

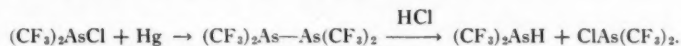
Analogous reactions have been used to prepare alkyl- and aryl-trifluoromethylarsines (3, 4):



Burg and Mahler (5) have reported that bistrifluoromethylphosphine can be prepared in 35% yield from the reaction of iodobistrifluoromethylphosphine with hydrogen chloride in the presence of mercury; other protic acids such as trifluoroacetic acid and phosphoric acid can be used. However, no bistrifluoromethylarsine is obtained when trifluoroacetic acid is used instead of hydrogen chloride. Burg and Mahler have suggested that the phosphine is formed through the following sequence:



but this does not easily account for the low yield of bistrifluoromethylphosphine or for the formation of chlorobistrifluoromethylphosphine. This scheme could apply to the present reaction though an alternative seems as likely:



Both these steps are possible since the reaction of chlorobistrifluoromethylarsine with mercury produces the diarsine quantitatively (2), and shaking the diarsine with excess hydrogen chloride and mercury produces bistrifluoromethylarsine in high yield. Such a mechanism, if it were the only one operating, would limit the yield of bistrifluoromethylphosphine to a maximum of 50% since chlorobistrifluoromethylphosphine does not react with mercury (6).

EXPERIMENTAL

Volatile reactants and products were manipulated in a glass vacuum system out of contact with oxygen and moisture. Chlorobistrifluoromethylarsine was prepared by reacting the corresponding iodoarsine with silver chloride (1). The product was distilled in a nitrogen atmosphere and boiled at 47° (lit. value, 46° (by extrapolation) (7)). Tetrakistrifluoromethyldiarsine was prepared by reducing chlorobistrifluoromethylarsine with mercury (2).

Reaction of Chlorobistrifluoromethylarsine with Hydrogen Chloride in the Presence of Mercury

The arsine (0.673 g), dry hydrogen chloride (0.729 g), and mercury (82 g), in a sealed tube (50 ml), were shaken at 23° for 17 hours. Trap-to-trap distillation gave only three fractions: tetrakistrifluoromethyldiarsine (0.067 g), which condensed at -78° and which was identified by its low vapor pressure (<20 mm at 23°) and by its infrared spectrum (1); bistrifluoromethylarsine (0.505 g, 86% yield), which condensed at -130° and which was identified by its molecular weight (found: 214, calc: 214) and by its infrared spectrum (1); hydrogen chloride (0.614 g), which condensed at -196°. No permanent gas was produced.

Reaction of Chlorobistrifluoromethylarsine with Trifluoroacetic Acid in the Presence of Mercury

The arsine (0.713 g), trifluoroacetic acid (7.6 g), and mercury (60.5 g), in a sealed tube (50 ml), were shaken at 23° for 40 hours. A slow reaction took place and eventually a considerable amount of white solid was deposited. Trap-to-trap distillation and infrared examination of the fractions isolated showed that no bistrifluoromethylarsine had been produced.

Reaction of Tetrakistrifluoromethyldiarsine with Hydrogen Chloride in the Presence of Mercury

The diarsine (1.128 g), hydrogen chloride (0.614 g), and mercury (63 g), in a sealed tube (50 ml), were shaken at 23° for 22 hours. Trap-to-trap distillation gave only three fractions: unreacted tetrakistrifluoromethyldiarsine (0.149 g), which condensed at -78°; bistrifluoromethylarsine (0.943 g, 84% yield), which condensed at -132°; and hydrogen chloride, which condensed at -196°. The fractions were identified as above. No permanent gas was produced.

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INTEGRAL HEATS OF MIXING OF C_6 -ALKANES IN PERFLUOROTRIBUTYLAMINE AND IN PERFLUOROCYCLIC OXIDE (C_3F_6O) AT 60° C

DAN E. NICHOLSON

In connection with studies of the thermodynamic properties of solutions of isomeric C_6 -hydrocarbons, the integral heats of mixing of these compounds have been determined in a perfluoroamine and a perfluoroether. The calorimeter and accessory apparatus were described previously (1). Provision was made in the calorimeter design for investigations of energy changes at elevated pressures and temperatures. Earlier studies of the experimental and theoretical heat effects involved in other fluorocarbon-hydrocarbon systems have been reported (2, 3, 4). Spectroscopic grade hydrocarbons obtained from the American Petroleum Institute were used without further purification. Perfluorocyclic oxide and perfluorotributylamine were purchased from the Minnesota Mining and Manufacturing Company under the designation FC-75 and FC-43, respectively. Both samples were purified by distillation in a 50-plate column so that the initial 20% and the final 20% portions were discarded.

Eight calorimetric experiments for each of the 10 binary solutions of the five hydrocarbons in the two solvents were performed covering the concentration range from 0.1

to 0.9 volume fractions. The integral heat of mixing data could be represented by an equation of the form

$$\Delta H = x_1 x_2 [-c_1 + c_2(x_1 - x_2) + c_3(x_1 - x_2)^2],$$

where

x = mole fraction of a component,

c = constant,

ΔH = endothermic integral heat of mixing, cal per mole of mixture, and subscript 1 refers to the hydrocarbon.

A summary of the experimental data is given in Table I. The constants shown will

TABLE I

	c_1	c_2	c_3
<i>n</i> -Hexane-(C ₄ F ₉) ₃ N	2182	349	2322
2-Methylpentane-(C ₄ F ₉) ₃ N	-2106	196	2444
3-Methylpentane-(C ₄ F ₉) ₃ N	-2170	66.8	2204
2,2-Dimethylbutane-(C ₄ F ₉) ₃ N	-2271	777	610
2,3-Dimethylbutane-(C ₄ F ₉) ₃ N	-2251	561	1538
<i>n</i> -Hexane-C ₈ F ₁₈ O	-2212	357	555
2-Methylpentane-C ₈ F ₁₈ O	-2274	614	191
3-Methylpentane-C ₈ F ₁₈ O	-2174	501	542
2,2-Dimethylbutane-C ₈ F ₁₈ O	-1967	607	508
2,3-Dimethylbutane-C ₈ F ₁₈ O	-2133	285	701

reproduce the calorimetric measurements within about $\pm 1\%$. The maximum endothermic integral heat of mixing calculated from the equation above is approximately 550 cal per mole of mixture in solutions equimolar in *n*-hexane and perfluorotributylamine.

One of the objectives of the present investigation was to determine whether or not useful empirical relationships involving the group-equivalent concept could be formulated to correlate the heats of mixing. For example, one may consider the heat of mixing of 2,3-dimethylbutane with a solvent to arise from contributions of two isopropyl groups. Likewise, for 2-methylpentane the observed heat effects could be attributable to isopropyl and *n*-propyl groups. An internally consistent set of relationships based upon this approach could not be developed. As an illustration of the application of the group-equivalent concept the values shown in Table II were estimated for the C₈F₁₈O-C₆H₁₄

TABLE II

Structural unit	Contribution to the heat of mixing in C ₈ F ₁₈ O as solvent at infinite dilution, cal/mole
H ₂ C-CH ₂ -CH ₂ ---	1055
$\begin{array}{c} \text{CH}_3 \\ \\ \text{H}_2\text{C}-\text{C}--- \\ \\ \text{H} \end{array}$	930
H ₂ C-CH ₂ ---	703
H ₂ C-CH ₂ -CH ₂ -CH ₂ ---	1406
$\begin{array}{c} \text{CH}_3 \\ \\ \text{H}_2\text{C}-\text{CH}_2-\text{CH}--- \end{array}$	1295
$\begin{array}{c} \text{CH}_3 \\ \\ \text{H}_2\text{C}-\text{C}--- \\ \\ \text{CH}_3 \end{array}$	1087

systems. The heats of mixing at infinite dilution were obtained by means of large-scale plots. The group-equivalent quantities for propyl, ethyl, and *n*-butyl structures were assigned from the heats of mixing of *n*-hexane. The value for the isopropyl group was derived from the appropriate quantities for 2-methylpentane and the propyl group. Similarly, for the *sec*-butyl structure, the group-equivalent value was obtained from 3-methylpentane while the *tert*-butyl structure was estimated from heats of mixing for 2,2-dimethylbutane. For 2,3-dimethylbutane the calculated heat of mixing is, therefore, 2×930 or 1860 cal/mole of hydrocarbon. The observed value for the heat of mixing is 2040 cal/mole.

Some comparisons between the experimental heat changes from the current work and those from regular solution theory (equation 17, p. 124, reference 5) have also been made. From solubility parameters and the appropriate molar volumes (3, 6) the values given in Table III are found for solutions in $C_8F_{16}O$ (solubility parameter = 5.9).

TABLE III

Mole fraction of <i>n</i> -hexane	ΔH (experimental), cal/mole of mixture	ΔE , cal/mole of mixture
0.2	350	48
0.4	515	78
0.6	560	84
0.8	450	61

Sufficient data are not available to test the more refined versions of the theoretical equations for predicting heats of mixing.

ACKNOWLEDGMENT

The writer is indebted to Mr. Theo Hines for assistance with experimental work.

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MOLECULAR ADDITION COMPOUNDS OF TRIOXAN

DOUGLAS HAMER AND JAMES LESLIE¹

Trioxan, the cyclic trimer of formaldehyde, is generally unreactive, but in the presence of acids, it is depolymerized to formaldehyde (1). For this reason trioxan is used in many organic reactions as an *in situ* source of formaldehyde, the formaldehyde being liberated by the addition of acid. No other chemical reactions of trioxan have been reported. This note describes the preparation of molecular addition compounds of this cyclic ether with

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picric acid and 1,3,5-trinitrobenzene. The derivative with 1,3,5-trinitrobenzene is a well-defined crystalline compound with a sharp melting point and may be of use in the classification and identification of trioxan. Trioxan did not form addition compounds with picrolonic acid or 1,2,7-trinitrofluorenone. Other cyclic ethers, e.g., dioxan and paraldehyde, did not form compounds with 1,3,5-trinitrobenzene or picric acid.

EXPERIMENTAL

Reaction of Trioxan with 1,3,5-Trinitrobenzene

Two grams of 1,3,5-trinitrobenzene was dissolved in slightly over the minimum quantity of boiling ethanol and 1.75 g of trioxan was added. Cooling of the solution caused the separation of pale yellow crystalline needles (2.6 g) which, on recrystallization from ethanol, yielded a compound of m.p. 94–97°. It was necessary to add a small amount of trioxan during the recrystallization; otherwise crystals of 1,3,5-trinitrobenzene separated. The addition compound could be similarly obtained in carbon tetrachloride, chloroform, or benzene. The derivative, however, did not readily precipitate from these solvents, but an apparently purer compound was obtained from carbon tetrachloride as pure white needles, m.p. 97°. Analysis: Found: C, 35.74; H, 2.92; N, 14.20; CH_2O , 30.16. $(\text{CH}_2\text{O})_3 \cdot \text{C}_6\text{H}_3(\text{NO}_2)_3$ requires: C, 35.65; H, 2.99; N, 13.86; CH_2O , 29.70. The analysis indicates a 1:1 molecular compound of trioxan and 1,3,5-trinitrobenzene.

Reaction of Trioxan with Picric Acid

A hot saturated solution of picric acid in ethanol was added to an almost saturated solution of trioxan in boiling ethanol. When the mixture was cooled, a bulky yellow mass which consisted mainly of trioxan, separated. The trioxan was removed by evaporation in air at room temperature, leaving a pale yellow residue, presumably a picrate of trioxan. This derivative decomposed on attempted recrystallization so no analysis was made. The melting point was 58°, and mixtures with trioxan and with picric acid melted at 40–60° and 60–90° respectively, suggesting that the derivative was indeed a compound of trioxan and picric acid.

All melting points are uncorrected.

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A SIMPLE REAGENT FOR THE SPECIFIC DEHYDRATION OF TERPENE ALCOHOLS*

E. VON RUDLOFF

The dehydration of terpene alcohols in the liquid phase with the common acidic reagents usually results in the formation of several isomeric olefins. This is undesirable both for structure determination and for preparative purposes. The dehydration of sesquiterpene alcohols with a weakly basic reagent, viz. thionyl chloride in the presence

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of excess pyridine, has been described recently by Motl *et al.* (1, 2), who obtained a mixture of isomeric hydrocarbons from both selin-4-ol and dihydro- α -cadinol. When this reagent was used in the current study with α -terpineol, dipentene (70%) and terpinolene (21%) were obtained and no other isomeric hydrocarbon was detected by gas-liquid chromatography (GLC). This is a considerable reduction in the number of isomers formed over that obtained when acidic reagents were used (3). However, because of the large excess of pyridine used with this reagent, the reaction is cumbersome. A much more convenient, and in some instances more specific, dehydration has now been obtained by heating the alcohol under reflux at 200 to 230° from 1 to 6 hours in the presence of twice its weight of neutral alumina (Woelm, activity grade I) to which 1 to 2% of pyridine or quinoline had been added. This reagent gave highly satisfactory results with α -terpineol, dihydro- α -terpineol, menthol, borneol, cedrol, and dihydroeudesmol, although the products obtained from linalool and isopulegol were more complex.

The amount of α -terpineol which had reacted with the reagent during 1 hour at 180°, 200°, and 220° C was 10%, 40%, and 82% respectively. The dehydration was virtually complete after 6 hours at 220° C, when dipentene (83%) and terpinolene (6%) were the only compounds detected by GLC. When α -terpineol was heated under reflux with neutral alumina alone, the steam-volatile product was found to be composed of α -terpinene (13%), dipentene (31%), *p*-cymene (16%), γ -terpinene (9%), terpinolene (26%), and *p*-mentha-2,4(8)-diene (5%), a composition very similar to that obtained with aqueous acidic reagents (2).

With dihydro- α -terpineol this base-modified alumina gave *trans*- (47%) and *cis*- (44%) *p*-menth-8-ene and *p*-menth-4(8)-ene (7%) after 1 hour reaction time. Since the ratio of *cis* to *trans* isomers in the starting material was 1:1 there appears to be no preferential reaction of either of the two isomers. Using the reagent of Motl *et al.* (1) the same mixture of hydrocarbons was obtained, but the yield of the *p*-menth-8-ene isomers was only 70%. Menthol, when treated with the new reagent for 1 hour, gave *p*-menth-2-ene (40%) and *p*-menth-3-ene (6%), whereas borneol was dehydrated to a mixture of camphene (68%) and tricyclene (16%). These results are very similar to those described by Pines and Pillai (4), who carried out the dehydration reaction of menthol, borneol, and neopentyl alcohol over ammonia-modified alumina in the gas phase. These authors propose that the dehydration takes place by a concerted mechanism involving both acidic and basic sites on the catalyst, whereas isomerization is suppressed by the preferential poisoning of the "strong acid sites" (5). Neutralization of acidic sites was confirmed in this study by evacuating the pyridine-treated alumina for 6 hours, when about 0.8% base was retained and no change in the reaction with α -terpineol was observed. Recently, Beranek *et al.* (6) have studied the dehydration of 4-methylcyclohexanol in the gas phase with a pyridine-modified alumina and have demonstrated that the active centers of the catalyst responsible for dehydration differ from those causing olefin isomerization. These authors also showed that, with unmodified alumina, isomerization is extensive and subsequent to dehydration. Thus there appears to be no difference in the reaction of tertiary or secondary alcohols over alumina catalysts in either the gas or liquid phase. The main feature of the base-modified alumina catalyst is the suppression of isomerization of the primary dehydration products by inhibiting carbonium-ion formation.

Dehydration of sesquiterpene alcohols with the new dehydrating agent also proceeds smoothly. Cedrol was converted to α -cedrene (85%) in 1 hour at 230° with only traces of an isomeric hydrocarbon being detected by GLC. When cedrol was treated with the thionyl chloride-pyridine reagent these two isomers were obtained in the ratio of 5:3. Dihydroeudesmol was similarly converted in high yield to a single hydrocarbon. Its

infrared spectrum had strong bands at 1645 and 880 cm^{-1} , showing it to be the isomer with the isopropenyl group. The dehydration of dihydroeudesmol with other reagents, as studied by Ruzicka *et al.* (7), produced invariably a mixture of dihydroeudesmene isomers. Thus it appears that the new reagent inhibits the formation of an exocyclic double bond, and it forms, therefore, an excellent complement to the common acidic reagents, which produce the exocyclic double bond preferentially in the early stages of the reaction.

The simplicity of the reaction with base-modified aluminas, however, does not seem to be general. Whereas the major reaction product with linalool was myrcene, four other hydrocarbons were detected in the reaction product. With isopulegol an even more complex mixture was obtained, nine hydrocarbon peaks and five peaks in the oxygenated terpene range being recorded by GLC. Since both of these alcohols are unstable at their boiling points, the formation of a complex mixture may be due to thermal decomposition or rearrangement rather than to the dehydration reaction itself. The reaction is being studied in more detail and the results obtained will be reported elsewhere.

EXPERIMENTAL

The gas chromatographic analyses were carried out with a modified Beckman GC-2 chromatograph. Quantitative data were obtained on the 12 ft \times $\frac{1}{8}$ in. (O.D.) rapeseed oil and 6 ft \times $\frac{1}{8}$ in. adipate and azelate polyester and polyethylene glycol columns described previously (2, 8, 9). The percentage composition was obtained by the triangulation method ($\pm 3\%$) and the average values are reported. The retention times of the sesquiterpenes and the *p*-menthenes are shown in Tables I and II. Those of the other compounds

TABLE I
Retention times* (in minutes) of sesquiterpenes at 180° C

Compound	Column:	Adipate polyester	Azelate polyester
	Flow rate (ml He/min):	58	43
α -Cedrene		3.6	5.8
Cedrene isomer		4.1	6.8
α -Cedrol		19.8	31.0
Dihydroeudesmene		3.5	5.6
Dihydroeudesmol		23.9	40.4
Eudesmol		27.6	46.0

*Measured at the initial emergence of the peaks.

TABLE II
Retention times* (in minutes) of *p*-menthenes at 80° C

Compound	Column:	Adipate polyester	Azelate polyester	Polyethylene glycol	Rapeseed oil
	Flow rate (ml He/min):	78	103	91	75
<i>p</i> -Menth-2-ene		3.1	4.5	4.8	60.0
<i>p</i> -Menth-3-ene		3.5	4.8	5.5	64.2
<i>p</i> -Menth-4(8)-ene		5.6	7.3	8.7	85.7
<i>p</i> -Menth-8-ene (trans)		3.9	5.2	6.4	67.2
<i>p</i> -Menth-8-ene (cis)		5.0	6.3	7.3	76.3
Limonene		8.2	12.1	13.3	99.6

*Measured at the initial emergence of the peaks.

have been reported earlier (9). Preparative runs were carried out as before on a 10- to 20-mg scale (2). The infrared spectra were recorded with a Perkin-Elmer model 21 double-beam spectrophotometer. Borneol, menthol, linalool, and isopulegol were commercial products, whereas dihydro- α -terpineol (50% trans and 50% cis) was prepared by hydrogenation of redistilled α -terpineol (99% pure), using platinum oxide as catalyst and methanol as solvent. Dihydroeudesmol, m.p. 85–86° C, $[\alpha]_D^{25} +18.0^\circ$ (CHCl₃), was obtained by a similar hydrogenation of eudesmol.

A typical dehydration experiment was carried out as follows. Neutral alumina (Woelm, activity grade I) (2.0 g) was placed into a 25-ml flask having two necks with ground-glass joints. To this was added pyridine (0.02 to 0.04 g) and α -terpineol (1.00 g) and the mixture was heated under reflux at 220° C (oil bath) for 6 hours. The mixture was then steam-distilled and the volatile product was taken up in a small volume of ether. After the ethereal solution had been dried over anhydrous sodium sulphate, it was transferred quantitatively to a flask having a long neck (2) and the ether was evaporated on a steam bath. The residue (0.79 g, 89% of theory) was analyzed by GLC. The composition of the hydrocarbons obtained was determined on the different columns at 80° C, and the amount of unreacted α -terpineol (in relation to the amount of hydrocarbons formed), at 110° or 130° C. The data obtained showed less than 1% unreacted alcohol, 93% dipentene, and 7% terpinolene. When quinolene was used as base instead of pyridine the respective yields of hydrocarbons were 92 and 6%.

In another experiment, neutral alumina (100.0 g) was thoroughly mixed with pyridine (2.0 g) and the mixture was evacuated to 0.5 mm Hg at room temperature for 6 hours. The residue (100.8 g) was used as such in the dehydration of α -terpineol, when practically identical results were obtained.

All other alcohols mentioned, except dihydroeudesmol, were dehydrated in the manner described in the first instance. Dihydroeudesmol (0.05 g) was weighed into a 10 cm \times 5 mm glass tube. To this was added pyridine-modified alumina (0.20 g) and the lower end of the tube was immersed into an oil bath at 230° C in such a manner that the upper half of the tube acted as an air condenser. After 1 hour the tube was cooled and the mixture was extracted with ether. The residue (0.03 g), after evaporation of the ether, was analyzed on the polyester columns at 160° and 180° C, when only a single hydrocarbon peak was recorded. The infrared spectrum was, therefore, recorded directly without further purification.

The dehydrations with thionyl chloride were carried out as follows. To the alcohol (1.00 g) was added dry pyridine (40 ml) and the solution was cooled to about 5° C. Thionyl chloride (3.0 g) was then added dropwise with shaking. After the mixture had been shaken for another 5 minutes, sodium carbonate (3 g) in water (15 ml) was added slowly. The mixture was extracted thrice with ether and the ethereal solution was washed with a saturated tartaric acid solution until all pyridine had been removed; pyridine was found to interfere with the GLC analysis. It was then washed with water and worked up as described above.

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SOLVENT EFFECTS ON THE RING PROTON MAGNETIC RESONANCE SPECTRA OF SOME SUBSTITUTED QUINOLINES

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Proton resonance spectra of unsaturated ring compounds are strongly solvent dependent. The spectra of substituted benzenes and heterocyclic compounds are affected both by the nature of the solvent and the degree of dilution (1, 2). The variation of the "internal" chemical shifts in these compounds in different solvents is surprisingly large since these systems are not generally regarded as involving either hydrogen bonding or other specific molecular association. Comparison of the shifts of the ring protons in these aromatic compounds in *n*-hexane, acetone, and benzene solvents leads to the conclusion that highly specific solute-solvent interactions are involved, at least in the benzene solutions. This note extends the experimental results to some substituted quinolines.

EXPERIMENTAL AND RESULTS

Dilute solutions of the compounds were made up to a uniform concentration of 5 mole% in *n*-hexane, benzene, and acetone. All measurements were made at 60 Mc/sec and peak positions were measured relative to an external chloroform reference.* Bulk susceptibility corrections were applied.

In Table I the shifts of the ring protons, corrected for bulk susceptibility differences, are tabulated relative to an external chloroform reference. The shifts are given only to the nearest cycles/sec because in many cases the analysis of the complex spectra did not allow a closer estimation. In some cases the benzene solvent peak obscured a few solute peaks but sometimes the preferential shifts caused by benzene allowed analysis of the spectra in benzene but not in *n*-hexane or acetone. An aid in the assignment of peaks was the fact that the ring protons ortho to a methyl or methylene group couple weakly to the latter protons. However, this also decreased the accuracy with which shifts and coupling constants could be extracted.

In Fig. 1 the proton shifts in *n*-hexane are taken as a reference point and the alterations of the shifts in the acetone and benzene solutions are plotted for all compounds. In Table II are given the coupling constants which could be obtained from the spectra. The estimated errors are relatively large because of the effects mentioned above.

*The calibrated spectra of the pure compounds and of the solutions are available upon request.

TABLE I

Shifts in cycles/sec at 60 Mc/sec from an external CHCl_3 reference (corrected for bulk susceptibility)
(Increasing shifts correspond to a higher magnetic field)

Compound	Solvent, 5 mole% solution in:	H ₂	H ₃	H ₄	H ₅	H ₆	H ₇	H ₈
Quinoline	<i>n</i> -Hexane	-79	20	-27	—	—	—	-36
	Acetone	-85	1.3	-37	—	—	—	-48
	Benzene	-53	66	21	—	—	—	-25
7-Ethylquinoline	<i>n</i> -Hexane	-78	23	-24	-4	13	—	-26
	Acetone	-85	4	-46	-22	0	—	-26
	Benzene	-59	61	13	25	—	—	-21
6,8-Dimethyl- quinoline	<i>n</i> -Hexane	-77	20	-20	12	—	12	—
	Acetone	-81	6	-37	4	—	4	—
	Benzene	-57	59	15	—	—	—	—
5,8-Dimethyl- quinoline	<i>n</i> -Hexane	-79	19	-36	—	23	11	—
	Acetone	-86	1	-51	—	13	2	—
	Benzene	-61	58	3	—	—	—	—
5,7-Dimethyl- quinoline	<i>n</i> -Hexane	-76	22	-34	—	26	—	-15
	Acetone	-83	5	-51	—	15	—	-14
	Benzene	-59	57	3	—	56	—	-12
4,6-Dimethyl- quinoline	<i>n</i> -Hexane	-66	31	—	-8	—	7	-30
	Acetone	-71	15	—	-20	—	-3	-27
	Benzene	-53	68	—	22	—	37	-27
3,8-Dimethyl- quinoline	<i>n</i> -Hexane	-72	—	-10	—	—	—	—
	Acetone	-78	—	-29	—	—	—	—
	Benzene	-58	—	28	—	—	—	—
2,8-Dimethyl- quinoline	<i>n</i> -Hexane	—	23	-19	—	—	—	—
	Acetone	—	8	-37	—	—	—	—
	Benzene	—	6	16	—	—	—	—

DISCUSSION

The preferential shifts of the ring protons at various positions relative to the polar group still await a satisfactory explanation. It is clear that a specific solute-solvent interaction is present, at least in benzene. In contrast to the substituted toluenes (1), however, we can observe the solution shifts of protons in both the meta (β) and para (γ) position (protons 3 and 4) to the nitrogen. From Table I and Fig. 1 it is clear that although proton 4 occurs to a much lower field than proton 3 in *n*-hexane solutions (resonance effect) its behavior in benzene and acetone solution parallels that of proton 3. Hence there is no simple relationship between charge density at the carbon to which the proton is bonded and the magnitude of the solvent shift for the proton. Qualitatively it is clear that the solvent effects increase as the distance between the negative nitrogen atom and the protons increases, but again there is no simple relationship since protons 5, 6, 7 are shifted less than protons 3 and 4 in benzene solutions. The shifts to high field of protons 5, 6, 7 are about 30 cycles/sec and this is about the value expected for the ordinary dilution shift in benzene due to the ring current effect (see reference 1). It follows that the higher shift for protons 3 and 4 must somehow be connected with the presence of the polar nitrogen although this connection is obscure. Since the π electrons of the benzene molecules are repelled by the negative nitrogen, it may be that the planar benzene molecules pack about the planar quinoline molecules in such a way as to avoid the nitrogen. This would explain why protons 2 and 8 are shifted to high field by a lesser amount than would be expected on the ring current effect of about 25-30 cycles/sec.

With one exception, the coupling constants in Table II have the values expected for ring protons. J_{23} is found to have a value of 4.0 ± 0.2 cycles/sec for all compounds, about half the value for a normal coupling constant between protons in the ortho position. This

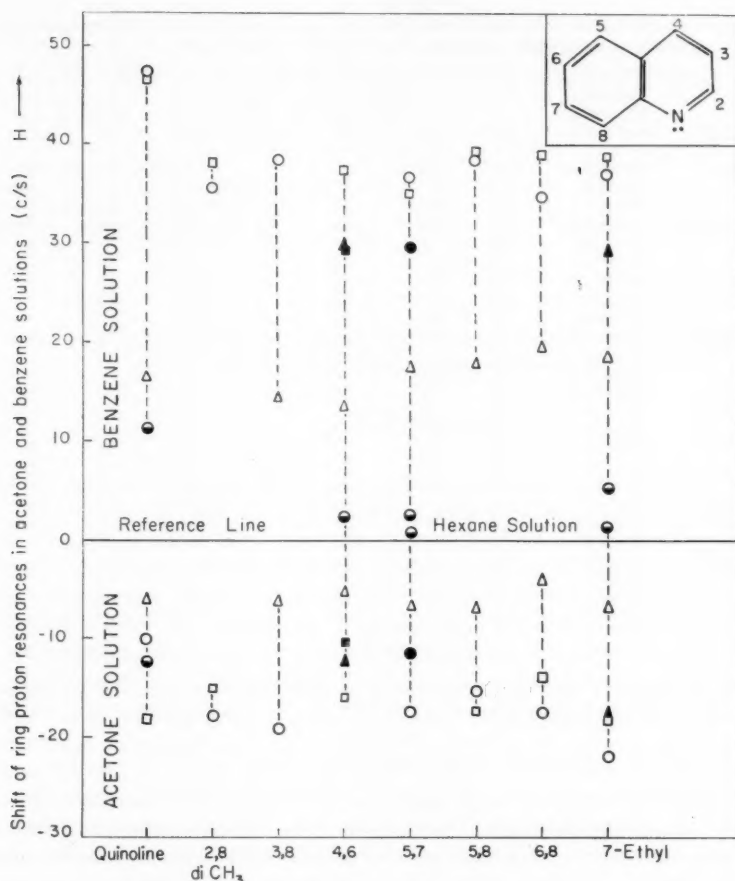


FIG. 1. Shifts of the ring protons of substituted quinolines in dilute acetone and benzene solutions relative to their position in the field for a dilute *n*-hexane solution. The shifts are given in cycles/sec for a measuring frequency of 60 Mc/sec. Δ , 2; \square , 3; \circ , 4; \blacktriangle , 5; \bullet , 6; \blacksquare , 7; \odot , 8.

value can be compared with one of 5.0 cycles/sec obtained from a spectrum of quinoline at 40 Mc/sec under somewhat lower resolution than was available in these experiments at 60 Mc/sec (3). Coupling of protons across the ring at positions 4 and 8 was found to be about 1 cycle/sec. Valence-bond calculations indicate coupling due to π electrons of less than 0.1 cycle/sec for the similar protons in naphthalene (4). Similar values have been found by Anet in 5,7-dimethylquinoline and 5,7-dichloroquinoline. As noted by Anet, such long-range coupling is limited to the 4- and 8-hydrogens and is comparable to coupling between hydrogen separated by five bonds in some olefins (5).

Finally, one might point out that in spectra as complex as these, preferential solvent shifts are extremely helpful in assignment of peaks as well as in the detailed analysis of groups of strongly coupled nuclei.

TABLE II
Coupling constants between ring protons in cycles/sec

Compound	J_{23}	J_{24}	J_{34}	J_{48}	J_{56}	J_{57}	J_{78}	J_{68}
Quinoline	4.1 ± 0.2	1.8 ± 0.2	8.5 ± 0.3	1.0 ± 0.2	—	—	8.2 ± 0.3	2.1 ± 0.2
2,8-Dimethylquinoline	4.2 ± 0.2	2.2 ± 0.2	—	—	—	—	—	—
4,6-Dimethylquinoline	—	—	—	—	—	1.8 ± 0.2	8.5 ± 0.2	—
5,7-Dimethylquinoline	4.0 ± 0.1	1.6 ± 0.1	8.4 ± 0.1	0.5	—	—	—	—
5,8-Dimethylquinoline	4.1 ± 0.1	1.7 ± 0.1	8.4 ± 0.2	—	—	7.2 ± 0.3	—	—
6,8-Dimethylquinoline	4.1 ± 0.1	1.8 ± 0.1	8.2 ± 0.2	—	—	—	—	—
7-Ethylquinoline	4.1 ± 0.1	1.8 ± 0.1	8.3 ± 0.2	0.8 ± 0.2	8.4 ± 0.1	—	—	—

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